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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

14 HOLOGIC, INC., CYTYC CORPORATION,
and HOLOGIC L.P.,

Plaintiffs,

vs.

SEGORX, INC.,

Defendant.

Case No. C08 00133 RMW (RS)

**DECLARATION OF KATHARINE L.
ALTEMUS IN SUPPORT OF PLAINTIFFS'
OPENING CLAIM CONSTRUCTION
BRIEF (PATENT L.R. 4-5(a))**

Markman Hearing
Date: June 25, 2008
Time: To Be Set
Room: Courtroom 6, 4th Floor
Judge: Hon. Ronald M. Whyte

AND RELATED COUNTERCLAIMS.

1 I, Katharine L. Altemus, declare that I am an associate in the law firm of Howrey LLP and a
2 member of the Bar of this court, and I serve as one of the outside counsel for Plaintiffs Hologic, Inc.,
3 Cytac Corporation and Hologic LP. The following declaration is based on my personal knowledge,
4 and if called upon to testify, I could and would competently testify as to the matters set forth herein.

5 1. Attached hereto as Exhibit A is a true and correct copy of United States Patent No.
6 5,913,813.

7 2. Attached hereto as Exhibit B is a true and correct copy of United States Patent No.
8 6,413,204.

9 3. Attached hereto as Exhibit C is a true and correct copy of United States Patent No.
10 6,482,142.

11 4. Attached hereto as Exhibit D is a true and correct copy of Defendant and
12 Counterclaimant Cytac Corporation's Opening Claim Construction Brief (Pat. L.R. 4-5(a)), filed in
13 *Xoft v. Cytac Corporation, et al.*, United States District Court, Northern District of California, Case
14 No. CV-05-05312 RMW on November 9, 2006, Docket No. 48.

15 5. Attached hereto as Exhibit E is a true and correct copy of Order Denying Plaintiffs'
16 Motion for Preliminary Injunction (Unredacted Version) Filed Under Seal in the within action on April
17 25, 2008, Docket No. 110.

18 6. Attached hereto as Exhibit F is a true and correct copy of Claim Construction Order,
19 filed in *Xoft v. Cytac Corporation, et al.*, United States District Court, Northern District of California,
20 Case No. CV-05-05312 RMW on April 27, 2007, Docket No. 109.

21 7. Attached hereto as Exhibit G is a true and correct copy of Plaintiffs' Notice of Motion
22 and Motion for Preliminary Injunction filed under seal in the within action on February 6, 2008,
23 Docket No. 8.

24 8. Attached hereto as Exhibit H is the Declaration of Lynn J. Verhey, Ph.D. In Support Of
25 Plaintiffs' Proposed Construction Of Claim Terms, Phrases And Clauses, with exhibits A, B, and C
26 thereto, signed on May 21, 2008.

27 \\

28

9. Attached hereto as Exhibit I is a true and correct copy of Amendment to Patent Application 08/900,021 dated September 1, 1998, on file with the United States Patent and Trademark Office, and part of the prosecution history of United States Patent No. 5,913,813.

4 10. Attached hereto as Exhibit J is a true and correct copy of Amendment to Patent
5 Application 09/464,727, dated February 27, 2002, on file with the United States Patent and Trademark
6 Office, and part of the prosecution history of United States Patent No. 6,482,142.

I declare under penalty of perjury that the foregoing is true and correct.

8 | Executed on May 21, 2008 at East Palo Alto, California

/s/

Katharine L. Altemus

EXHIBIT A

United States Patent [19]

Williams et al.

[11] Patent Number: 5,913,813

[45] Date of Patent: Jun. 22, 1999

[54] **DOUBLE-WALL BALLOON CATHETER FOR TREATMENT OF PROLIFERATIVE TISSUE**

[75] Inventors: **Jeffery A. Williams**, Baltimore, Md.; **Christopher H. Porter**, Woodinville, Wash.; **Jeffrey F. Williamson**; **James F. Dempsey**, both of St. Louis, Mo.; **Timothy J. Patrick**; **James B. Stubbs**, both of Alpharetta, Ga.

[73] Assignee: **Proxima Therapeutics, Inc.**, Alpharetta, Ga.

[21] Appl. No.: 08/900,021

[22] Filed: Jul. 24, 1997

[51] Int. Cl.⁶ A61N 5/00

[52] U.S. Cl. 600/3

[58] Field of Search 600/1-8

[56] **References Cited**

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3,324,847 6/1967 Zoumboulis .

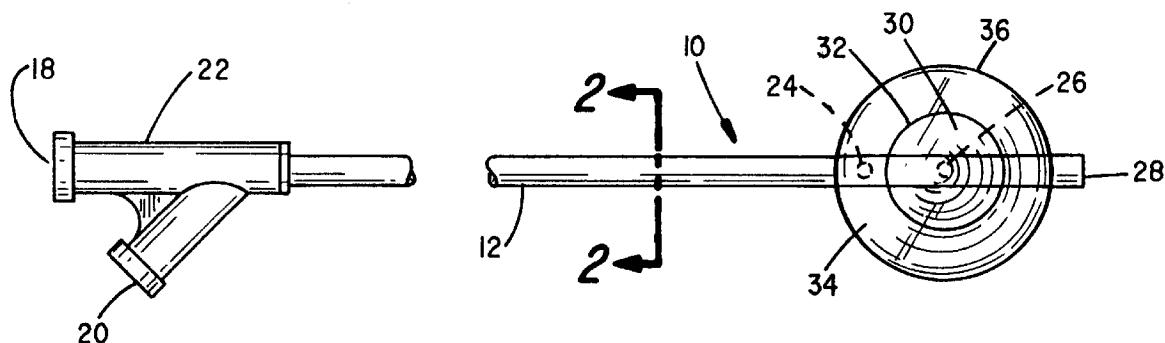
5,106,360	4/1992	Ishiwara et al. .
5,429,582	7/1995	Williams .
5,611,767	3/1997	Williams .
5,662,580	9/1997	Bradshaw et al. 600/3
5,782,742	7/1998	Crocker et al. .
5,785,688	7/1998	Joshi et al. .

Primary Examiner—John P. Lacy
Attorney, Agent, or Firm—Nikolai, Mersereau & Dietz, P.A.

[57] **ABSTRACT**

An instrument for use in brachytherapy comprises a concentric arrangement of inner and outer distensible, spherical chambers disposed near the proximal end of a catheter body where one of the chambers is made to contain a radioactive material with the other chamber containing a radiation absorptive material, the apparatus functioning to provide a more uniform absorbed dose profile in tissue surrounding a cavity created by the removal of a tumor. An alternative embodiment includes non-spherical inner and outer chambers whose respective walls are spaced equidistant over the entire surfaces thereof.

13 Claims, 2 Drawing Sheets



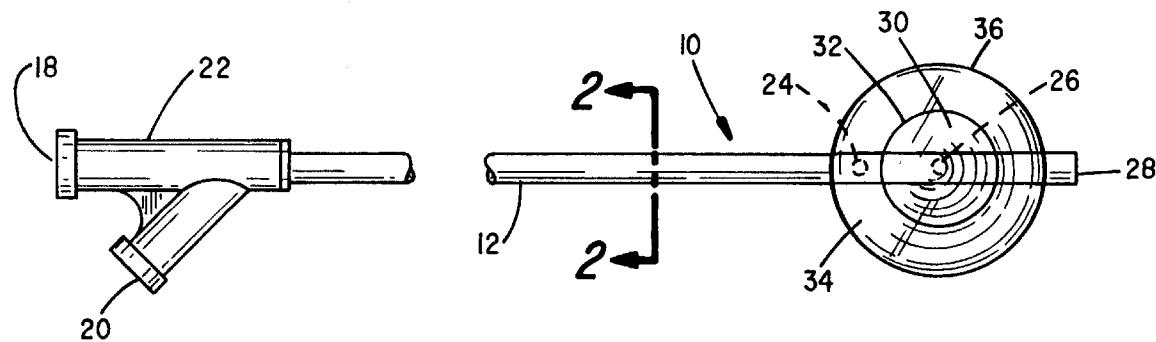


FIG. 1

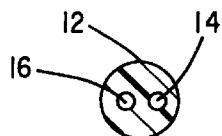


FIG. 2

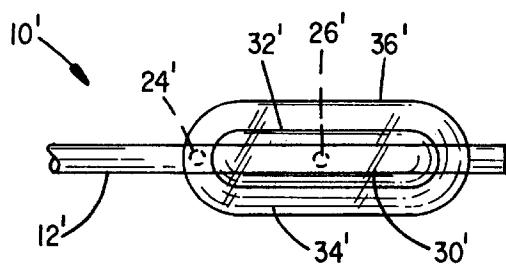


FIG. 3

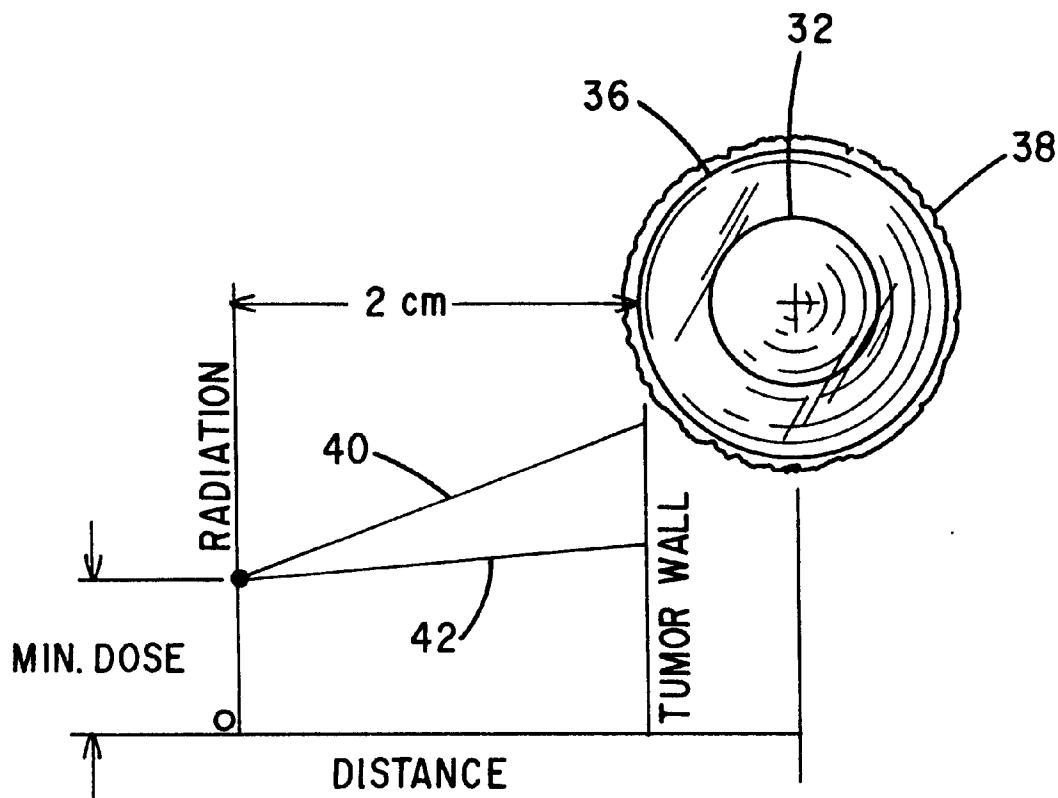


FIG. 4

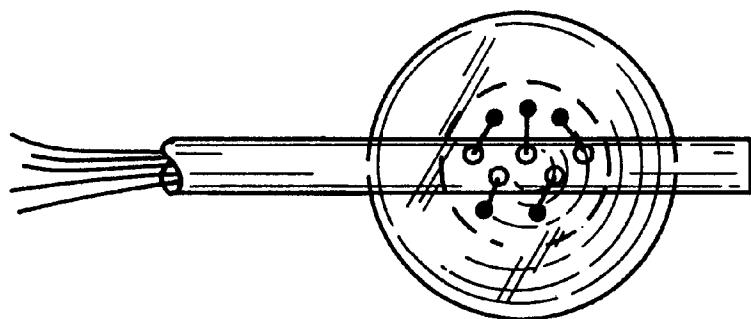


FIG. 5

DOUBLE-WALL BALLOON CATHETER FOR TREATMENT OF PROLIFERATIVE TISSUE**BACKGROUND OF THE INVENTION****I. Field of the Invention**

This invention relates generally to apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radioactive material and/or radiation emissions.

II. Discussion of the Prior Art

In the Williams U.S. Pat. No. 5,429,582 entitled "Tumor Treatment", there is described a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the margins surrounding the excised tumor. In accordance with that patent, there is provided a catheter having an inflatable balloon at a distal end thereof to define a distensible reservoir. Following surgical removal of a tumor, say in the brain or breast, the deflated balloon may be introduced into the surgically-created pocket left following removal of a tumor and then the balloon is inflated by injecting a fluid having radionuclide(s) therein into the distensible reservoir, via a lumen in the catheter.

When it is considered that the absorbed dose rate at a point exterior to the radioactive source is inversely proportional to the square of the distance between the radiation source and the target point, tissue directly adjacent the wall of the distensible reservoir may be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that is delivered to a site 0-3 cms away from the wall of the excised tumor. It is desirable to keep the radiation in the space between that site and the wall of the distensible reservoir as uniform as possible to prevent over-exposure to tissue at or near the reservoir wall. In treating other cancers, such as bladder cancer, where the neoplastic tissue is generally located on the bladder surface, deep penetration is unnecessary and to be avoided.

A need exists for an instrument which may be used to deliver radiation from a radioactive source to target tissue within the human body of a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target.

SUMMARY OF THE INVENTION

We have found that it is possible to deliver a desired radiation dose at a predetermined radial distance from a source of radioactivity by providing a first spacial volume at the distal end of a catheter and a second spacial volume defined by a surrounding of the first spacial volume by a polymeric film wall where the distance from the spatial volume and the wall is maintained substantially constant over their entire surfaces. One of the inner and outer volumes is filled with either a fluid or a solid containing a radionuclide(s) while the other of the two volumes is made to contain either a low radiation absorbing material, e.g., air or even a more absorptive material, such as an x-ray contrast fluid. Where the radioactive material comprises the core, the surrounding radiation absorbing material serves to control the radial profile of the radioactive emissions from the particular one of the inner and outer volumes containing the radionuclide(s) so as to provide a more radially uniform radiation dosage in a predetermined volume surrounding the

outer chamber. Where the core contains the absorbent material, the radial depth of penetration of the radiation can be tailored by controlling the core size.

DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. 1 is a side view of an apparatus for delivering radioactive emissions to body tissue;

FIG. 2 is a cross-sectional view taken along the line **2—2** in FIG. 1;

FIG. 3 is a fragmentary side view of an apparatus for administering radiation therapy in accordance with a second embodiment;

FIG. 4 is a graph helpful in understanding the operation of the apparatus of the present invention; and

FIG. 5 depicts a further embodiment of the invention.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring first to FIG. 1, there is indicated generally by numeral **10** a surgical instrument for providing radiation treatment to proliferative tissue in a living patient. It is seen to comprise a tubular body member **12** having first and second lumens **14** and **16** (FIG. 2) extending from proximal ports **18** and **20** in a molded plastic hub **22** to inflation ports **24** and **26** formed through the side wall of the tube **12** and intersecting with the lumens **14** and **16**, respectively.

Affixed to the tubular body **12** proximate the distal end **28** thereof is an inner spatial volume **30** which may be defined by a generally spherical polymeric film wall **32**. The interior of the chamber **30** is in fluid communication with the inflation port **26**. Surrounding the spatial volume **30** is an outer chamber **34** defined by an outer polymeric film wall **36** that is appropriately spaced from the wall **32** of the inner chamber **30** when the two chambers are inflated or otherwise filled and supported. Chamber **34** encompasses the inflation port **24**.

The embodiment of FIG. 1 can be particularly described as comprising two spherical chambers **30** and **34**, one inside the other. In accordance with a first embodiment of the invention, the outer chamber **34**, being the volume defined by the space between the inner spherical wall **32** and the outer spherical wall **36**, may be filled with air or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. The inner chamber **30** is then filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles or other therapeutic rays.

Those skilled in the art will appreciate that instead of having the inner spatial volume **30** defined by a generally spherical polymeric film wall as at **32**, the catheter body member **12** may have a solid spherical radiation emitting material in which event that solid sphere would be surrounded with the outer spherical wall **36** with the spatial volume therebetween occupied by a radioactive ray absorbent material, such as air, water or a contrast material.

It is further contemplated that instead of having the inner spatial volume comprising a single solid sphere, it may instead comprise a plurality of radioactive particles strategically placed within the inner spatial volume so as to radiate

in all directions with a substantially equal intensity. FIG. 5 illustrates a catheter having the inner spatial volume occupied by a plurality of radioactive beads that are mounted on the distal ends of a plurality of wires that are routed through the catheter body and exit a plurality of ports formed through the wall of the catheter body and reaching the lumen. This arrangement allows the exact positioning of the individual radiation sources to be positioned so as to generate a desired resultant profile.

It is not essential to the invention that the chambers 30 and 34 have spherical walls, so long as the spacing between the wall of the inner chamber and the wall of the outer chamber remain generally constant, such as is illustrated in FIG. 3.

Referring to FIG. 4, there is shown the two concentric spherical chambers of FIG. 1 defined by inner spherical wall 32 and outer spherical wall 36 disposed within the margin 38 of a surgically excised tumor. It is desired that the radiation emitted from the core 32 be capable of delivering a certain minimum dose absorbed at a location approximately 0–3 cms from the margin 38. Curve 40 is a plot of absorbed dose vs. radial distance that would be obtained if the inner chamber defined by spherical wall 32 was not present and the entire volume of the spherical chamber defined by wall 36 were filled with the radioactive fluid. Plot 42 reflects the absorbed dose distribution as a function of radial distance when the radioactive fluid is contained within the inner chamber and is surrounded by either a gas or a more radiation absorbing material. Comparing the plots 40 and 42, by providing the concentric arrangement depicted, the absorbed dose profile in the space between the 2 cm site and the wall of the outer balloon is maintained much more uniform, thus preventing over-treatment of body tissue at or close to the outer wall 36 of the instrument. That is to say, to obtain the same end point absorbed dose at 2 cm, it would be necessary to increase the source activity relative to that used for a completely filled (to surface 36) configuration, assuming the same radionuclide is used in both configurations.

With no limitation intended, the distensible polymeric chambers may comprise a biocompatible, radiation resistant polymer, such as Silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, PVC, C-Flex. The radioactive fluid contained within the inner chamber 32 can be made from any solution of radionuclide(s), e.g., a solution of I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel.

In the embodiments heretofore described, the material containing the radionuclide(s) is located in the inner chamber. The invention also contemplates that the outer chamber 34 may contain the material having the radionuclide therein while the inner chamber 30 contains the radiation absorptive material. This configuration is advantageous where a profile exhibiting higher intensity at a tissue surface with lesser penetration is desired. By using this approach, less volume of radioactive material is required than if the entire volume of the device were filled with radioactive material. Moreover, the outer chamber wall need not be spherical, yet a uniform profile is obtainable. Experiments have shown that a steeper radial absorbed source gradient can be obtained using a radiation attenuation fluid in the inner chamber 30 than otherwise obtains when only a single distensible chamber is used, as in the aforereferenced Williams U.S. Pat. No. 5,429,582. The invention also contemplates that the radioactive material in the inner core can be replaced by a core containing solid radionuclide-containing

particles. For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used in place of the fluid. This radioactive source can either be preloaded into the catheter at the time of manufacture or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. Such a solid radioactive core configuration offers the advantage in that it allows a wider range of radionuclides than if one is limited to liquids. Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources.

In either the concentric spherical embodiment of FIG. 1 or the non-spherical configuration of FIG. 3, the spacing between the inner and outer chambers needs to be held somewhat constant to avoid "hot spots". This result can be achieved by careful placement of precision blown polymer parisons or by using compressible foams or mechanical spacers in the form of webs joining the inner wall 32 to the outer wall 36.

This invention has been described herein in considerable detail in order to comply with the patent statutes and to provide those skilled in the art with the information needed to apply the novel principles and to construct and use such specialized components as are required. However, it is to be understood that the invention can be carried out by specifically different equipment and devices, and that various modifications, both as to the equipment and operating procedures, can be accomplished without departing from the scope of the invention itself.

What is claimed is:

1. Apparatus for delivering radioactive emissions to a body location with a uniform radiation profile, comprising:
 - (a) a catheter body member having a proximal end and distal end;
 - (b) an inner spatial volume disposed proximate the distal end of the catheter body member;
 - (c) an outer, closed, inflatable, chamber defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall;
 - (d) a material containing a radionuclide(s) disposed in one of the inner spatial volume and outer chamber; and
 - (e) means disposed in the other of the inner spatial volume and outer chamber for rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber containing the radionuclides.
2. The apparatus as in claim 1 wherein said inner spatial volume is an inner closed, chamber defined by a further radiation transparent wall.
3. The apparatus of claim 1 wherein the means for rendering uniform the absorbed dose profile is a radiation attenuating material.
4. The apparatus of claim 3 wherein the radiation attenuating material is selected from a group consisting of barium sulphate, water, and X-ray contrast media.
5. The apparatus as in claim 2 wherein the radionuclide is in a fluid form.
6. The apparatus as in claim 5 wherein the fluid comprises an isotope of iodine.
7. The apparatus as in claim 1 wherein the radionuclide is a slurry of a fluid containing particles of a solid isotope.

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8. The apparatus as in claim 2 wherein the inner chamber contains the radioactive material.

9. The apparatus as in claim 1 wherein the outer chamber contains the radioactive material.

10. The apparatus as in claim 8 wherein the radioactive material is a fluid.

11. The apparatus as in claim 8 wherein the radioactive material is a solid.

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12. The apparatus as in claim 1 wherein the material containing a radionuclide comprises a plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile.

13. The apparatus as in claim 2 wherein the inner and outer chambers are spherical in shape and are concentric.

* * * * *

EXHIBIT B

(12) United States Patent
Winkler et al.(10) Patent No.: US 6,413,204 B1
(45) Date of Patent: *Jul. 2, 2002

(54) INTERSTITIAL BRACHYTHERAPY APPARATUS AND METHOD FOR TREATMENT OF PROLIFERATIVE TISSUE DISEASES

(75) Inventors: Rance A. Winkler, Atlanta; Timothy J. Patrick; James Stubbs, both of Alpharetta, all of GA (US)

(73) Assignee: Proxima Therapeutics, Inc., Alpharetta, GA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: 09/293,524

(22) Filed: Apr. 15, 1999

Related U.S. Application Data

(63) Continuation-in-part of application No. 08/900,021, filed on Jul. 4, 1997, now Pat. No. 5,913,813.

(51) Int. Cl.⁷ A61N 5/00

(52) U.S. Cl. 600/3

(58) Field of Search 600/1-8

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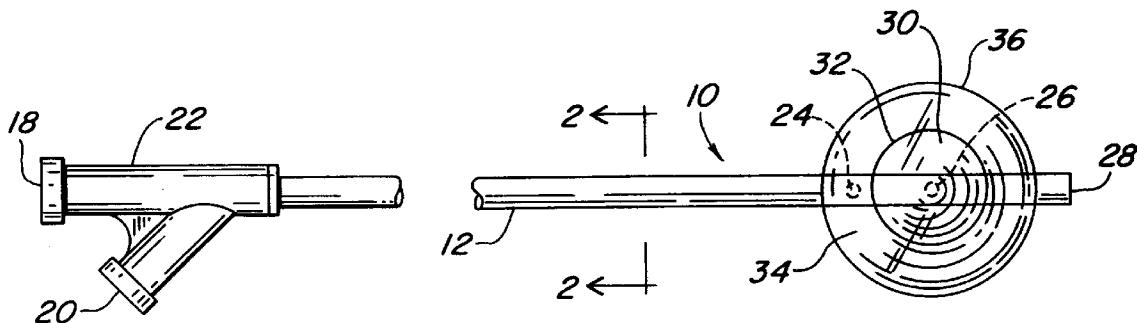
Primary Examiner—John P. Lacyk

(74) Attorney, Agent, or Firm—Thomas J. Engellenner; Ronald E. Cahill; Nutter, McClellan & Fish, LLP

(57) ABSTRACT

An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location includes a catheter body member having a proximal end and distal end, an inner spatial volume disposed proximate to the distal end of the catheter body member, an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume, and a radiation source disposed in the inner spatial volume.

36 Claims, 3 Drawing Sheets



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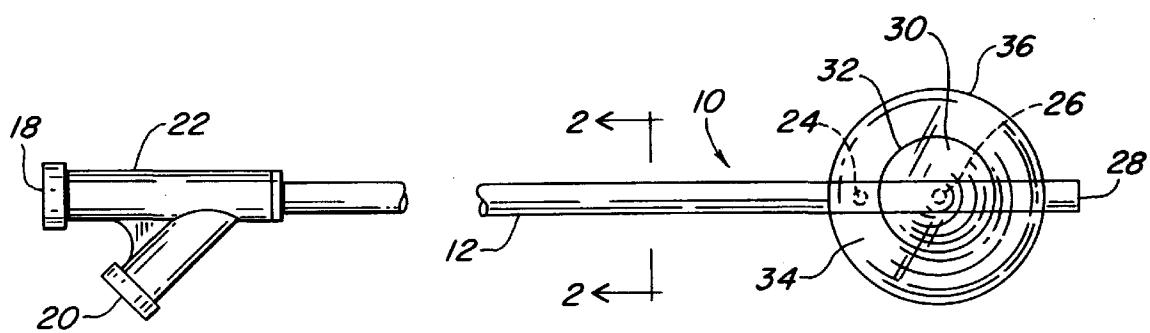


FIG. 1

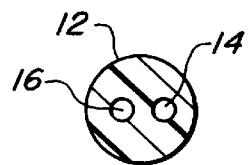


FIG. 2

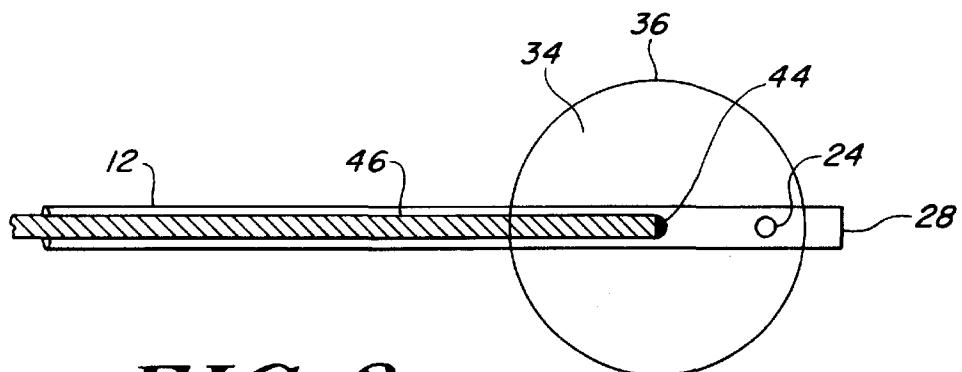


FIG. 3

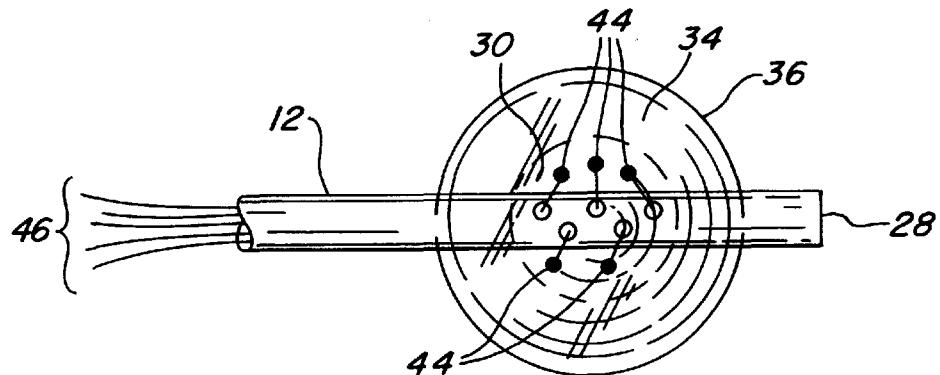


FIG. 4

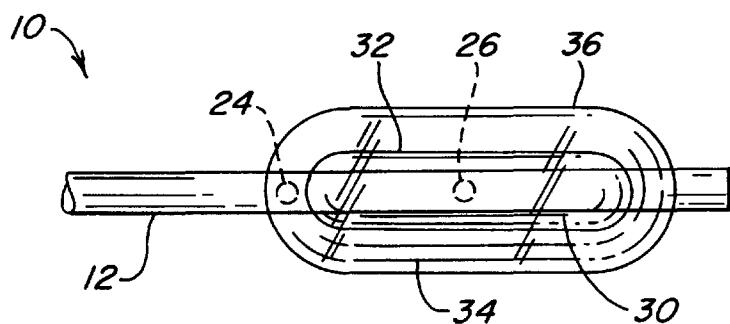


FIG. 5

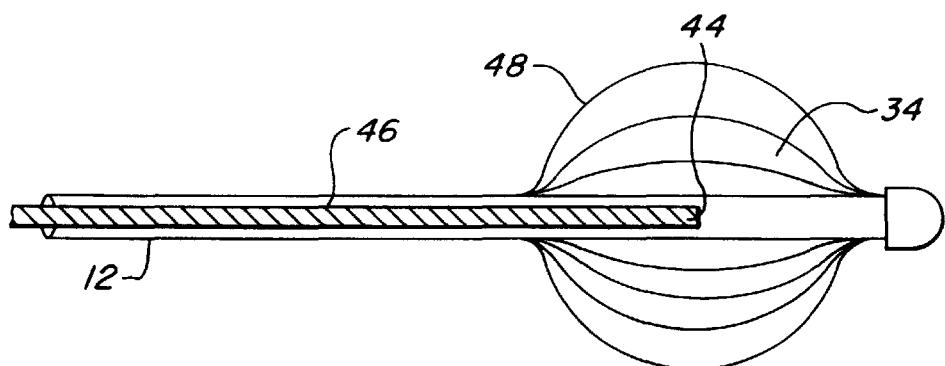


FIG. 6

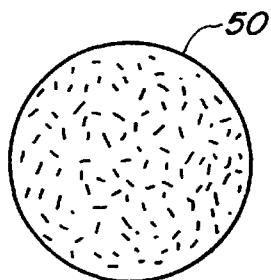


FIG. 7A

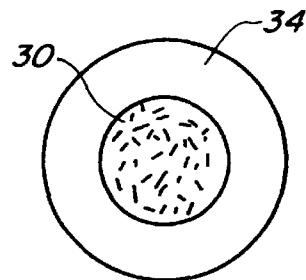


FIG. 7B

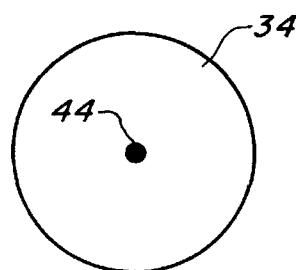


FIG. 7C

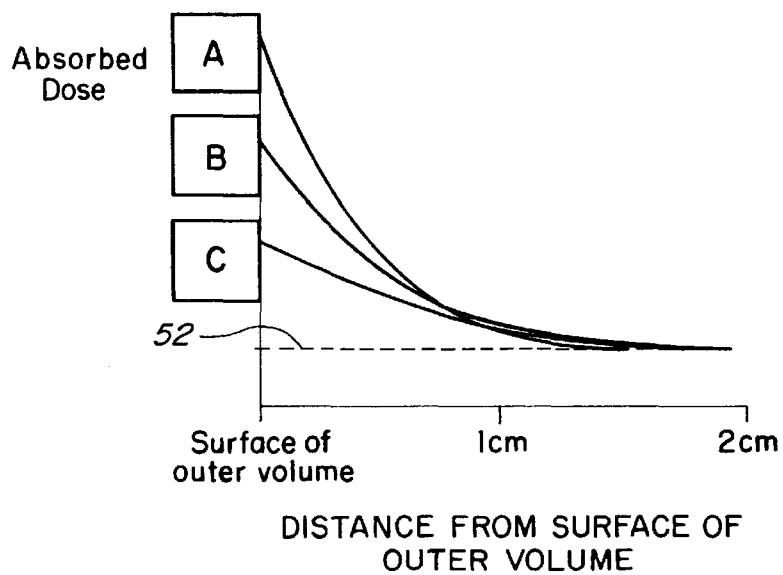


FIG. 7D

1

**INTERSTITIAL BRACHYTHERAPY
APPARATUS AND METHOD FOR
TREATMENT OF PROLIFERATIVE TISSUE
DISEASES**

**CROSS-REFERENCE TO RELATED
APPLICATIONS**

This application is a continuation-in-part of U.S. patent application Ser. No. 08/900,021, filed Jul. 24, 1997, now U.S. Pat. No. 5,913,813 the contents of which are specifically incorporated herein by reference.

BACKGROUND OF THE INVENTION

The invention relates generally to apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radiation.

Malignant tumors are often treated by surgical resection of the tumor to remove as much of the tumor as possible. Infiltration of the tumor cells into normal tissue surrounding the tumor, however, can limit the therapeutic value of surgical resection because the infiltration can be difficult or impossible to treat surgically. Radiation therapy can be used to supplement surgical resection by targeting the residual tumor margin after resection, with the goal of reducing its size or stabilizing it. Radiation therapy can be administered through one of several methods, or a combination of methods, including external-beam radiation, stereotactic radiosurgery, and permanent or temporary interstitial brachytherapy. The term "brachytherapy," as used herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site. Owing to the proximity of the radiation source, brachytherapy offers the advantage of delivering a more localized dose to the target tissue region.

For example, brachytherapy is performed by implanting radiation sources directly into the tissue to be treated. Brachytherapy is most appropriate where 1) malignant tumor regrowth occurs locally, within 2 or 3 cm of the original boundary of the primary tumor site; 2) radiation therapy is a proven treatment for controlling the growth of the malignant tumor; and 3) there is a radiation dose-response relationship for the malignant tumor, but the dose that can be given safely with conventional external beam radiotherapy is limited by the tolerance of normal tissue. In brachytherapy, radiation doses are highest in close proximity to the radiotherapeutic source, providing a high tumor dose while sparing surrounding normal tissue. Interstitial brachytherapy is useful for treating malignant brain and breast tumors, among others.

Interstitial brachytherapy is traditionally carried out using radioactive seeds such as ¹²⁵I seeds. These seeds, however, produce inhomogeneous dose distributions. In order to achieve a minimum prescribed dosage throughout a target region of tissue, high activity seeds must be used, resulting in very high doses being delivered in some regions in proximity to the seed or seeds which can cause radionecrosis in healthy tissue.

Williams U.S. Pat. No. 5,429,582, entitled "Tumor Treatment," describes a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the tissue surrounding the excised tumor. In order to implement the radioactive emissions, Williams provides a catheter having an inflatable balloon at its distal end that defines a

2

distensible reservoir. Following surgical removal of a tumor, the surgeon introduces the balloon catheter into the surgically created pocket left following removal of the tumor. The balloon is then inflated by injecting a fluid having one or 5 more radionuclides into the distensible reservoir via a lumen in the catheter.

The apparatus described in Williams solves some of the problems found when using radioactive seeds for interstitial brachytherapy, but leaves some problems unresolved. The 10 absorbed dose rate at a target point exterior to a radioactive source is inversely proportional to the square of the distance between the radiation source and the target point. As a result, where the radioactive source has sufficient activity to deliver a prescribed dose, say 2 centimeters into the target tissue, the 15 tissue directly adjacent the wall of the distensible reservoir, where the distance to the radioactive source is very small, may still be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that 20 is delivered to a region up to about two centimeters away from the wall of the excised tumor. It is desirable to keep the radiation that is delivered to the tissue in the target treatment region within a narrow absorbed dose range to prevent over-exposure to tissue at or near the reservoir wall, while 25 still delivering the minimum prescribed dose at the maximum prescribed distance from the reservoir wall.

There is still a need for an instrument which can be used to deliver radiation from a radioactive source to target tissue 30 within the human body with a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target.

SUMMARY OF THE INVENTION

The present invention solves the problems described above by providing an interstitial brachytherapy apparatus 35 for delivering radioactive emissions to an internal body location. The apparatus includes a catheter body member having a proximal end and distal end, an inner spatial volume disposed proximate to the distal end of the catheter body member, an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume, and a radiation source disposed in the inner spatial volume. The inner and outer spatial volumes are configured to provide an absorbed dose within a predetermined range throughout a target tissue. The target tissue is located between the outer spatial volume expandable surface 40 and a minimum distance outward from the outer spatial volume expandable surface. The predetermined dose range is defined as being between a minimum prescribed absorbed dose for delivering therapeutic effects to tissue that may include cancer cells, and a maximum prescribed absorbed dose above which healthy tissue necrosis may result.

In different embodiments, the inner spatial volume can be defined by a distensible polymeric wall containing radioactive source material which can be a fluid material, by a solid radioactive source, or by a region containing a plurality of 45 solid radioactive sources. The outer spatial volume is defined by an expandable surface element that may be, for example, an inflatable polymeric wall or an expandable cage. The expandable surface element can cause tissue to conform to its intended shape, and preferably, the apparatus creates absorbed isodose profiles in the target tissue that are substantially similar in shape to the expandable surface element in substantially three dimensions.

The invention also provides a method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location. The method includes surgically creating access to the proliferating tissue within a patient and surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue. An interstitial brachytherapy apparatus for delivering radioactive emissions as described above is then provided and intra-operatively placed into the resection cavity. After a prescribed absorbed dose has been delivered to tissue surrounding the apparatus, the apparatus is removed. The radioactive source material may be placed into the interstitial brachytherapy apparatus after the apparatus is placed in the resection cavity, and may be removed before the apparatus is removed. The method has particular applications to brain and breast cancers.

DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. 1 is a side view of an interstitial brachytherapy apparatus of the invention for delivering radioactive emissions to body tissue;

FIG. 2 is a cross-sectional view taken along the line 2—2 in FIG. 1;

FIG. 3 is an additional embodiment of an interstitial brachytherapy apparatus of the invention having a solid radiation source;

FIG. 4 is an additional embodiment of an interstitial brachytherapy apparatus of the invention having a radiation source comprising a plurality of solid radiation particles;

FIG. 5 depicts a further embodiment of the invention wherein the inner and outer spatial volumes of the interstitial brachytherapy apparatus are non-spherical;

FIG. 6 illustrates an interstitial brachytherapy apparatus of the invention having an expandable outer spatial volume surface; and

FIGS. 7A-D illustrate the absorbed dose versus distance into target tissue for several interstitial brachytherapy apparatus configurations.

DESCRIPTION OF THE PREFERRED EMBODIMENT

A surgical instrument 10 for providing radiation treatment to proliferative tissue in a living patient is illustrated in FIG. 1. Surgical instrument 10 includes a tubular body member 12 having first and second lumens 14 and 16 (FIG. 2) extending from proximal ports 18 and 20 in a molded plastic hub 22 to inflation ports 24 and 26 formed through the side wall of the tube 12 and intersecting with the lumens 14 and 16, respectively.

Affixed to the tubular body 12 proximate the distal end 28 thereof is an inner spatial volume 30 which may be defined by a generally spherical polymeric film wall 32. The interior of the inner volume 30 is in fluid communication with the inflation port 26. Surrounding inner spatial volume 30 is an outer spatial volume 34 defined by an outer polymeric film wall 36 that is appropriately spaced from the wall 32 of the inner spatial volume 30 when the two volumes are inflated or otherwise supported. Outer volume 34 encompasses inflation port 24. With no limitation intended, the distensible polymeric film walls may comprise a biocompatible, radia-

tion resistant polymer, such as silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, or PVC.

The embodiment of FIG. 1 includes inner and outer spatial volumes 30 and 34, one inside the other. The outer spatial volume 34, being the volume defined by the space between the inner spherical wall 32 and the outer spherical wall 36, may be filled with air or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. The inner volume 30 is then filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles, gamma radiation, or other therapeutic rays. The radioactive material contained within the inner chamber 32 can be a fluid made from any solution of radionuclide(s), e.g., a solution of I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel. One radioactive material useful in the invention is Iotrex™, a sterile single use, non-pyrogenic solution containing sodium 3-(¹²⁵I)iodo-4-hydroxybenzenesulfonate (¹²⁵I-HBS), available from Proxima Therapeutics, Inc. of Alpharetta, Ga.

As an alternative method of providing radioactive source material, such material may be coated on, chemically bonded to, or copolymerized with the material forming inner spherical wall 32.

Where the radioactive source material is provided as a fluid or gel within inner spherical wall 32, it may be desirable to provide a solid outer spherical wall 36. Should inner spherical wall 32 rupture, the radioactive source material will be retained within outer spherical wall 36 and will not leak into the patient. For further safety, the burst strength of inner spherical wall 32 may be designed so as to be lower than that of outer spherical wall 36. In this way, inner spherical wall 32 will rupture under stress first, releasing its contents into the larger combined space of the inner and outer volumes 30, 34 and releasing any pressure built up within the inner spherical wall 32 and reducing the risk that radioactive material will spill into the patient. In the event of such a rupture, radioactive fluid could be drained from the apparatus through port 24 by way of lumen 14, and also from port 26 by way of lumen 16.

In a further embodiment, illustrated in FIG. 3, instead of having the inner spatial volume 30 defined by a generally spherical polymeric film wall as at 32, the catheter body member 12 may have a solid spherical radiation emitting material 44 as the inner spatial volume 30. For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used. This radioactive source can either be preloaded into the catheter at the time of manufacture or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. The solid radiation emitting material 44 can be inserted through catheter 12 on a wire 46, for example, using an afterloader (not shown). Such a solid radioactive core configuration offers an advantage in that it allows a wider range of radionuclides than if one is limited to liquids. Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources. In this embodiment solid spherical inner spatial volume 30 is surrounded by outer spherical wall 36, defining outer spatial volume 34 between the outer spherical wall 36 and the inner spatial volume 30 with the outer spatial volume 34 occupied by a radioactive ray absorbent material, such as air, water or a contrast material.

In a further embodiment, illustrated in FIG. 4, inner spatial volume 30, instead of comprising a single solid sphere, may comprise a plurality of radiation emitting particles 44 strategically placed within the inner spatial volume 30 so as to radiate in all directions with a substantially equal intensity. This plurality of radiation emitting particles 44 can be mounted on the distal ends of a plurality of wires 46 that are routed through the catheter body 12 and exit a plurality of ports formed through the wall of the catheter body and reaching the lumen. This arrangement allows the exact positioning of the individual radiation sources 44 to be positioned so as to generate a desired resultant profile.

As illustrated in FIG. 5, it is not essential to the invention that the volumes 30 and 34 have spherical walls, so long as the resultant dosing profile is consistent with the shape of the outer volume 34. That is, the absorbed dose within the target tissue at points equidistant from the surface 36 of the outer spatial volume 34 should be substantially uniform in substantially every direction. Put another way, the three dimensional isodose profiles generated by the radiation source should be substantially similar in shape to the outer spatial volume 34. Where the inner and outer spatial volumes are created by inflatable membranes and one of the volumes contains a fluid radiation source, this can be achieved by ensuring that the spacing between the wall of the inner volume and the wall of the outer volume remain generally constant. In either the concentric spherical embodiment of FIG. 1 or the non-spherical configuration of FIG. 5, this result can be achieved by careful placement of precision blown or molded polymer partitions or by using compressible foams or mechanical spacers in the form of webs joining the inner wall 32 to the outer wall 36. The desired isodose profiles conforming to the shape of the outer spatial volume 34 can also be obtained, for example, by strategic placement of a plurality of radioactive particle sources within the inner spatial volume 30. Where the apparatus of the invention is deployed in soft tissue, it may also be important for the surface 36 of the outer spatial volume 34 to be sufficiently firm so as to force the target tissue to take on the shape of the surface 36 so that the desired relationship between the isodose profiles and the target tissue is achieved.

When used in an interstitial application, the surface of the outer spatial volume 34 must establish a relationship between the inner spatial volume 30 and the target tissue so as to achieve the aforementioned isodose profile, however, the surface of the outer volume need not be a solid material. For example, as illustrated in FIG. 6, the surface of the outer volume 34 could be an expandable cage 48 formed from a shape memory metal, such as nitinol, or a suitable plastic, such as an expandable polyethylene cage. Such a cage can be formed in the desired shape to conform to a particular isodose profile, then be contracted for delivery to the target site *in vivo*, then expanded to cause the tissue surrounding the surgically resected region to take the appropriate shape. The size of the outer spatial volume 34 generally will correspond approximately to the amount of tissue resected, or be slightly larger, allowing the expandable surface of the outer spatial volume to urge tissue on the surface of the resected region into the appropriate shape to promote an even dose distribution around the outer spatial volume in the target tissue. In typical applications, the outer spatial volume has a diameter of approximately 2 to 4 centimeters. In these same applications, where the radiation source is provided as a fluid within an inner balloon, the inner balloon generally has a diameter of approximately 0.5 to 3 centimeters.

FIGS. 7A-D illustrate the ability of an interstitial brachytherapy apparatus of the invention to deliver a minimum

prescribed dose within target tissue while avoiding necrosis inducing radiation "hot spots" in tissue proximate to the apparatus. FIG. 7A illustrates an interstitial brachytherapy apparatus (device A) such as those employed in U.S. Pat. No. 5,429,582, having a single spatial volume 50 filled with a radioactive material in solution. FIG. 7B illustrates an interstitial brachytherapy apparatus (device B) of the invention having a first, inner spatial volume 30 filled with a radioactive material in solution and defined by membrane 32, and a second, outer spatial volume 34 defined by membrane 36 that is substantially evenly spaced apart from membrane 32 in substantially three dimensions. FIG. 7C illustrates an additional interstitial brachytherapy apparatus (device C) of the invention having a solid, spherical radiation source 44 as the inner spatial volume and a spherical outer spatial volume 34 defined by membrane 36.

Each of the devices illustrated in FIGS. 7A-C can be configured to deliver a substantially uniform dose at a given distance into the target tissue from the surface of the outer spatial volume 34 (or from single spatial volume 50 for device A) and to deliver a minimum prescribed dose within a given prescribed depth range into the tissue from the surface of the outer spatial volume 34. However, the different devices provide very different dose profiles as a function of distance from the surface of the outer volume as illustrated in FIG. 7D. FIG. 7D plots the absorbed dose at a given distance into the target tissue from the surface of the outer spatial volume 34 for each of the devices A, B, and C.

Each device can deliver a minimum prescribed dose 52 at a given distance from the surface of the outer spatial volume. For example, device A can readily be configured to provide a dose in a therapeutic range, say between 40 to 60 Gray, at a distance between 0.5 and 1.0 cm from the outer spatial volume for an outer spatial volume having a diameter of 4.0 cm and being in contact with the resection cavity wall. In a typical embodiment, the radioactive source material ranges from approximately 150 to 450 mCi in activity and encompasses most of the target treatment area with a 0.4 to 0.6 Gray/hour isodose contour. At this treatment rate, treatment may be completed in approximately 3 to 7 days, or more commonly, in approximately 3 to 5 days.

In order to reach the minimum prescribed dosage at this distance, however, device A must provide a dose proximate to the surface of the outer spatial volume that is substantially larger than the minimum prescribed dose. For the 4.0 cm diameter outer spatial volume example, the absorbed dosage would be approximately 131 Gray at the outer spatial volume surface. Ideally, radiation therapy should make use of the inherent difference in radiosensitivity between the tumor and the adjacent normal tissues to destroy cancerous tissue while causing minimal disruption to surrounding normal tissues. At high doses of radiation, however, the percentage of exposed cells that survive treatment decreases with first-order kinetics in proportion to increasing radiation dose. With increasing cell death comes increasing risk of necrosis or tissue death in healthy tissue that is treated with a high dose of radiation. Accordingly, it is desirable to keep the maximum radiation dose delivered by the brachytherapy apparatus as low as possible while still delivering the desired therapeutic dose to the desired range of tissue.

Comparing the plots A, B, and C, the absorbed dose profile in the space between the 2 cm site and the surface of the outer spatial volume for the devices of the invention is maintained in a much narrower range, preventing over-treatment of body tissue at or close to the surface of the outer volume of the device. Because devices B and C provide an outer spatial volume 34 between the radioactive source and

the target tissue, these devices can use hotter radiation sources to reach the minimum prescribed dosage, but take advantage of the distance between the radioactive source and the target tissue provided by the outer spatial volume 34 to reduce or eliminate hot spots in the target tissue.

Returning to the 4.0 cm diameter outer spatial volume example, if the radiation source is contained within an inner spatial volume, say a solid radioactive sphere such as device C, the absorbed dose profile becomes much different. If the radiation source is configured to provide the same 60 Gray dose at 0.5 cm into the target tissue, the absorbed dose at the outer spatial volume surface is only 94 Gray—a significant decrease from the 131 Gray dose for a type A device. In addition, the treatment range for the type C device will be extended under these circumstance as compared to the type A device, delivering a 40 Gray dose beyond 1.0 cm into the target tissue and delivering approximately double the dose at 3.0 cm into the target tissue. In one embodiment, the inner and outer spatial volumes are configured to control the absorbed dose at the outer spatial volume surface so that the absorbed dose is no greater than about 100 Gray while providing a therapeutic absorbed dose into the target tissue at the desired range. The capability of the apparatus of the invention to deliver absorbed doses deeper into the target tissue than prior interstitial brachytherapy devices while controlling the dose in proximity to the apparatus to reduce or eliminate the risk of healthy tissue necrosis allows for the use of brachytherapy in a greater number of cases. 25

The interstitial brachytherapy apparatus of the invention can be used in the treatment of a variety of malignant tumors, and is especially useful for in the treatment of brain and breast tumors.

Many breast cancer patients are candidates for breast conservation surgery, also known as lumpectomy, a procedure that is generally performed on early stage, smaller tumors. Breast conservation surgery is typically followed by postoperative radiation therapy. Studies report that 80% of breast cancer recurrences after conservation surgery occur near the original tumor site, strongly suggesting that a tumor bed “boost” of local radiation to administer a strong direct dose may be effective in killing any remaining cancer and preventing recurrence at the original site. Numerous studies and clinical trials have established equivalence of survival for appropriate patients treated with conservation surgery plus radiation therapy compared to mastectomy.

Surgery and radiation therapy are the standard treatments for malignant solid brain tumors. The goal of surgery is to remove as much of the tumor as possible without damaging vital brain tissue. The ability to remove the entire malignant tumor is limited by its tendency to infiltrate adjacent normal tissue. Partial removal reduces the amount of tumor to be treated by radiation therapy and, under some circumstances, helps to relieve symptoms by reducing pressure on the brain.

A method according to the invention for treating these and other malignancies begins by surgical resection of a tumor site to remove at least a portion of the cancerous tumor and create a resection cavity. Following tumor resection, but prior to closing the surgical site, the surgeon intra-operatively places an interstitial brachytherapy catheter apparatus, having an inner spatial volume and an outer spatial volume as described above but without having the radioactive source material loaded, into the tumor resection cavity. Once the patient has sufficiently recovered from the surgery, the interstitial brachytherapy catheter is loaded with a radiation source. The radioactive source dwells in the catheter until the prescribed dose of radiotherapy is

delivered, typically for approximately a week or less. The radiation source is then retrieved and the catheter is removed. The radiation treatment may end upon removal of the brachytherapy apparatus, or the brachytherapy may be supplemented by further doses of radiation supplied externally. 5

It will be understood that the foregoing is only illustrative of the principles of the invention, and that various modifications can be made by those skilled in the art without departing from the scope and spirit of the invention. All references cited herein are expressly incorporated by reference in their entirety. 10

What is claimed is:

1. An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

- (a) a catheter body member having a proximal end and distal end;
- (b) an inner spatial volume disposed proximate to the distal end of the catheter body member;
- (c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
- (d) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

2. The apparatus of claim 1, wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface. 30

3. The apparatus of claim 2, wherein a predetermined spacing is provided between said inner spatial volume and the expandable surface element. 35

4. The apparatus of claim 3, wherein the expandable surface element is adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element. 40

5. The apparatus of claim 2, wherein the minimum prescribed absorbed dose is 40 Gray at a distance of at least one centimeter from the expandable surface element. 45

6. The apparatus of claim 5, wherein the dose rate in at least a portion of the target tissue is between about 0.4 and 0.6 Gray/hour. 50

7. The apparatus of claim 5, wherein the maximum absorbed dose delivered to the target tissue is less than 100 Gray. 55

8. The apparatus of claim 2, wherein the outer spatial volume has a diameter between about two and four centimeters. 60

9. The apparatus of claim 2, wherein the inner spatial volume is an inner closed, distensible chamber defined by a further radiation transparent wall. 65

10. The apparatus of claim 9, wherein the radioactive source is in a fluid form.

11. The apparatus of claim 10, wherein the expandable surface element is a solid distensible surface and the outer spatial volume is a closed, distensible chamber and the expandable surface element is a radiation transparent wall. 65

12. The apparatus of claim 11, wherein a burst strength of the distensible chamber defining the outer spatial volume is greater than a burst strength of the chamber defining the inner spatial volume.

13. The apparatus of claim 1, wherein the expandable surface element is an expandable cage.

14. The apparatus of claim 13, wherein the expandable cage comprises a shape memory material.

15. The apparatus of claim 14, wherein the expandable cage comprises nitinol.

16. The apparatus of claim 1, wherein the radiation source is a solid radiation source.

17. The apparatus of claim 1, wherein the radiation source is a plurality of solid radiation sources arranged to provide an isodose profile having a shape substantially similar to the shape of the outer spatial volume.

18. The apparatus of claim 2, wherein the prescribed absorbed dose is delivered to the target tissue in substantially three dimensions.

19. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

- (a) surgically creating access to the proliferating tissue in a patient;
- (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;
- (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (iv) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element;
- (d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity until a prescribed absorbed dose has been delivered to tissue surrounding the apparatus; and
- (e) removing the interstitial brachytherapy apparatus.

20. The method of claim 19, further including placing the radioactive source into the interstitial brachytherapy apparatus after the step of placing the apparatus into the tumor resection cavity.

21. The method of claim 19, further including removing the radioactive source from the interstitial brachytherapy apparatus before the step of removing the apparatus.

22. The method of claim 19, wherein the proliferating tissue is a patient's brain.

23. The method of claim 19, wherein the proliferating tissue is a patient's breast.

24. The method of claim 19, further including configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

25. The method of claim 24, further including providing a predetermined spacing between said inner spatial volume and the expandable surface element.

26. The method of claim 25, wherein the expandable surface element is adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element.

27. The method of claim 24, wherein the minimum prescribed absorbed dose is 40 Gray at a distance of at least one centimeter from the expandable surface element.

28. The method of claim 27, wherein the dose rate in at least a portion of the target tissue is between about 0.4 and 0.6 Gray/hour.

29. The method of claim 27, wherein the maximum absorbed dose delivered to the target tissue is less than 100 Gray.

30. The method of claim 24, wherein the outer spatial volume has a diameter between about two and four centimeters.

31. The method of claim 24, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

32. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

- (a) surgically creating access to the proliferating tissue in a patient;
- (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;
- (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (iv) a radiation source disposed in the inner spatial volume;
- (d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;
- (e) configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface; and
- (f) removing the interstitial brachytherapy apparatus.

33. The method of claim 32, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

34. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

- (a) surgically creating access to the proliferating tissue in a patient;
- (b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;

11

- (c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:
 - (i) a catheter body member having a proximal end and distal end;
 - (ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (iv) a radiation source disposed in the inner spatial volume;
- (d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;
- (e) adapting the expandable surface element to contact tissue surrounding the resection cavity to conform the tissue to the desired shape of the expandable surface element;
- (f) delivering a prescribed absorbed dose to tissue surrounding the apparatus; and
- (g) removing the interstitial brachytherapy apparatus.

35. The method of claim 34, wherein the step of adapting the expandable surface element includes expanding the outer surface volume.

12

- 36. An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:
 - (a) a catheter body member having a proximal end and distal end;
 - (b) an inner spatial volume disposed proximate to the distal end of the catheter body member;
 - (c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and
 - (d) a radiation source disposed in the inner spatial volume;
- wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

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EXHIBIT C

(12) United States Patent
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(45) Date of Patent: Nov. 19, 2002

(54) ASYMMETRIC RADIATION DOSING APPARATUS AND METHOD

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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Related U.S. Application Data

(63) Continuation-in-part of application No. 09/293,524, filed on Apr. 15, 1999, which is a continuation-in-part of application No. 08/900,021, filed on Jul. 24, 1997, now Pat. No. 5,913,813.

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(52) U.S. Cl. 600/3

(58) Field of Search 600/1-8

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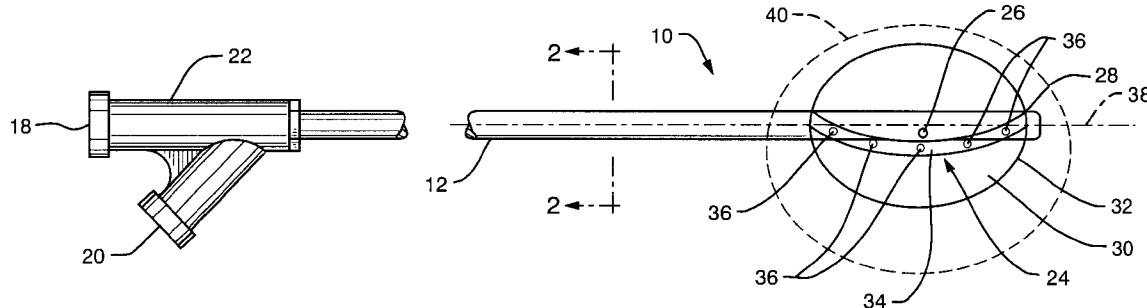
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(57) ABSTRACT

An interstitial brachytherapy apparatus of the invention delivers radioactive emissions in an asymmetric fashion to target tissue surrounding a surgical extraction site. The apparatus includes an expandable outer surface element defining an apparatus spatial volume, a radiation source disposed within the apparatus volume, and a means for providing predetermined asymmetric isodose curves within the target tissue. In one configuration, asymmetric isodose curves are created in the target tissue by shaping or locating the radiation source so as to be asymmetrically placed with respect to a longitudinal axis of the apparatus. In other configurations, asymmetric radiopaque shielding is provided between the radiation source and the target tissue. A surgical procedure using the apparatus is also described.

14 Claims, 4 Drawing Sheets

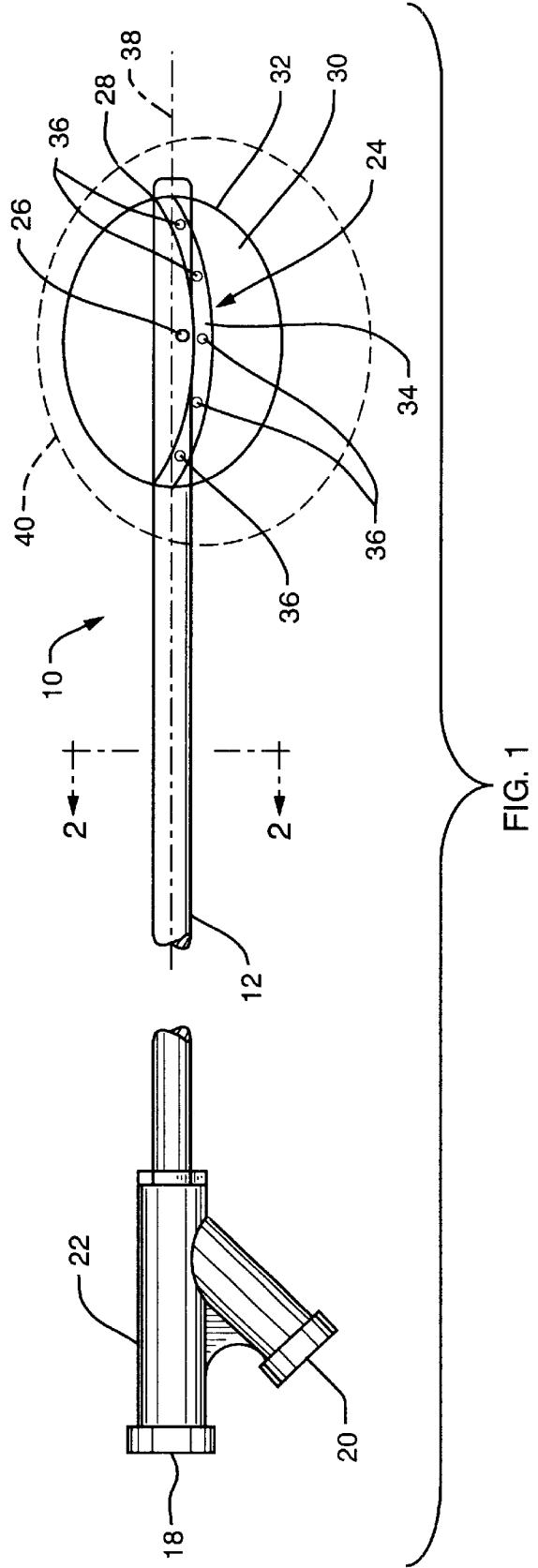


FIG. 1

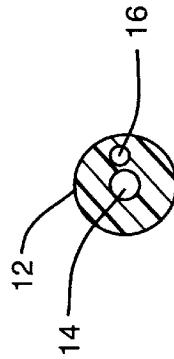
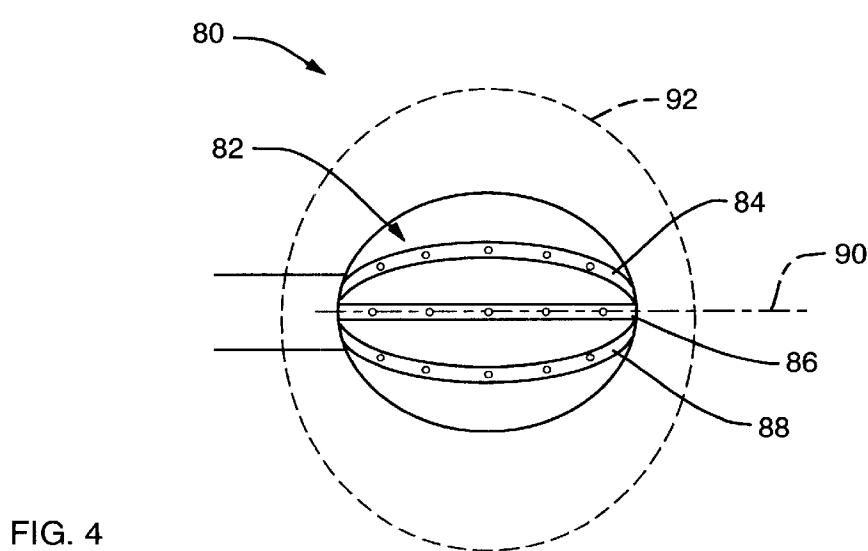
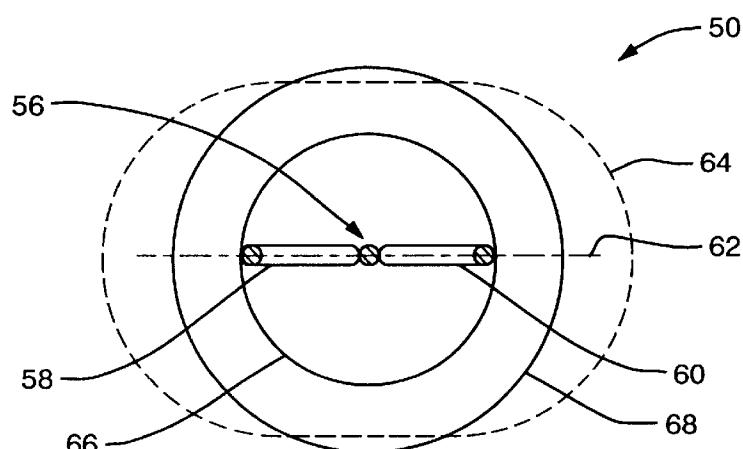
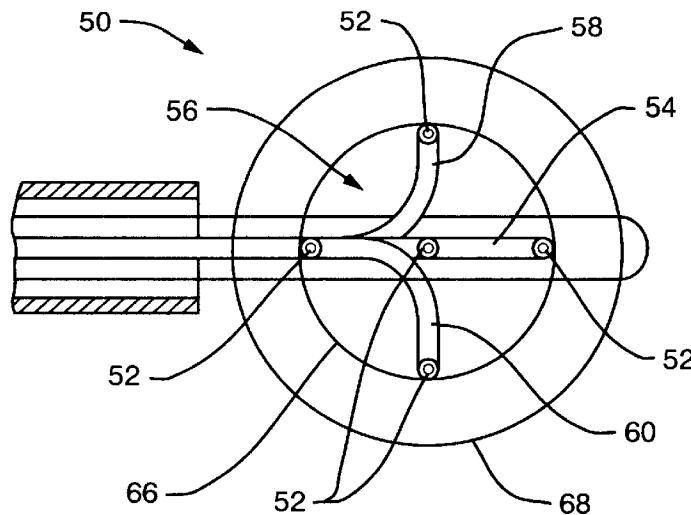


FIG. 2



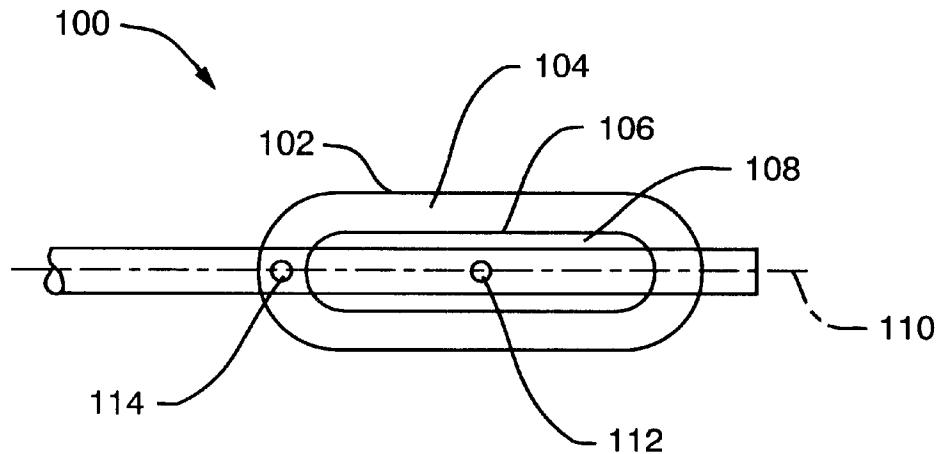


FIG. 5

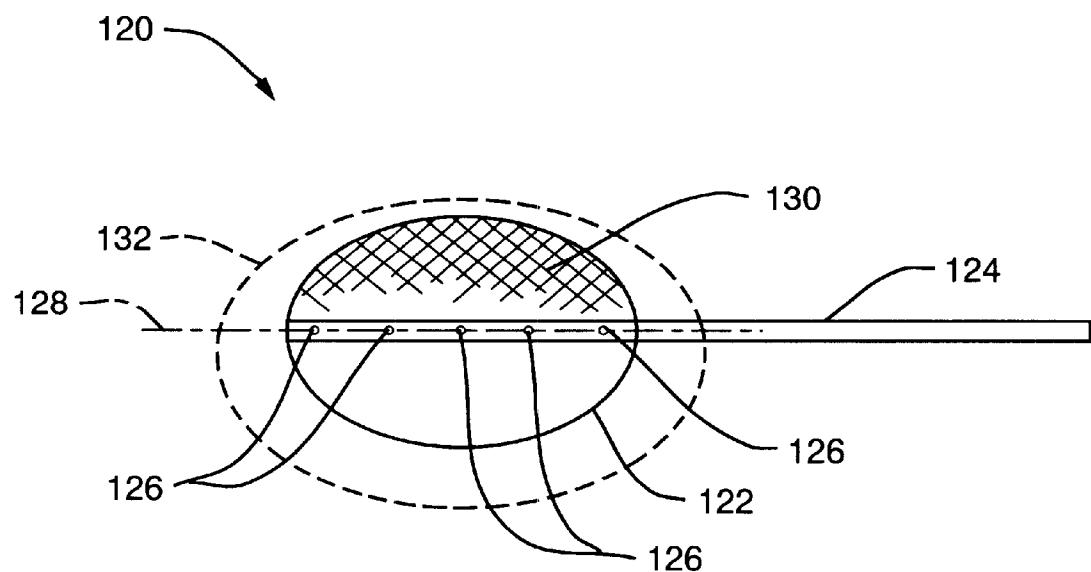


FIG. 6

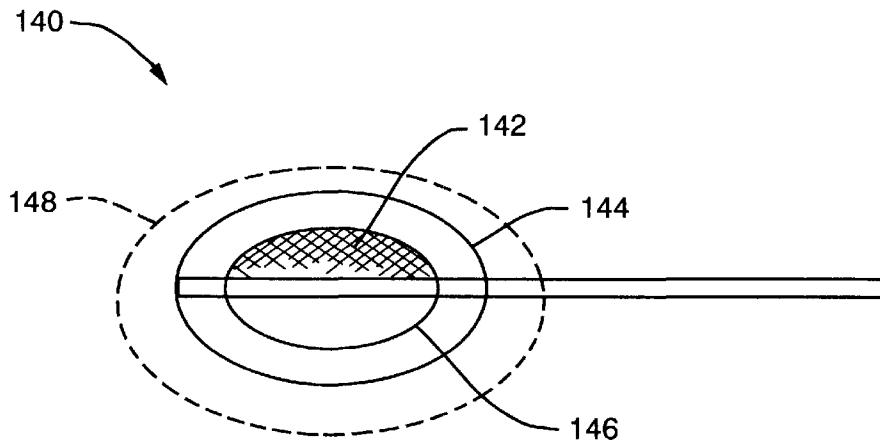


FIG. 7

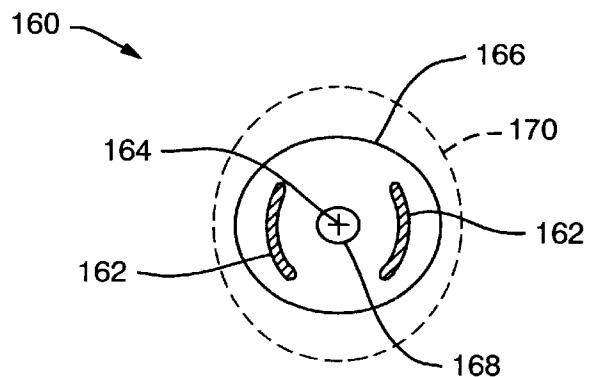


FIG. 8

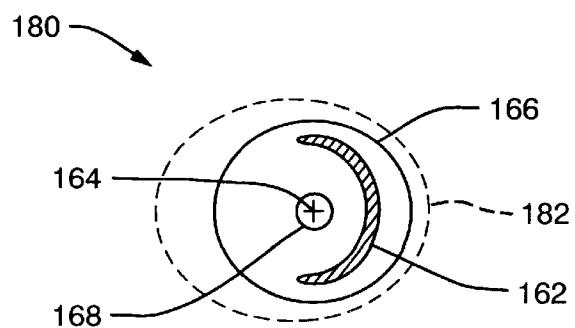


FIG. 9

1

**ASYMMETRIC RADIATION DOSING
APPARATUS AND METHOD**

**CROSS-REFERENCE TO RELATED
APPLICATIONS**

This application is a continuation-in-part of co-pending U.S. patent application Ser. No. 09/293,524, filed Apr. 15, 1999, pending which is a continuation-in-part U.S. patent application Ser. No. 08/900,021, filed Jul. 24, 1997 (now issued as U.S. Pat. No. 5,913,813 to Williams et al.); the contents of these applications are specifically incorporated herein by reference.

BACKGROUND OF THE INVENTION

The invention relates generally to an apparatus for use in treating proliferative tissue disorders, and more particularly to an apparatus for the treatment of such disorders in the body by the application of radiation.

Malignant tumors are often treated by surgical resection of the tumor to remove as much of the tumor as possible. Infiltration of the tumor cells into normal tissue surrounding the tumor, however, can limit the therapeutic value of surgical resection because the infiltration can be difficult or impossible to treat surgically. Radiation therapy can be used to supplement surgical resection by targeting the residual tumor margin after resection, with the goal of reducing its size or stabilizing it. Radiation therapy can be administered through one of several methods, or a combination of methods, including external-beam radiation, stereotactic radiosurgery, and permanent or temporary interstitial brachytherapy. The term "brachytherapy," as used herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site. Owing to the proximity of the radiation source, brachytherapy offers the advantage of delivering a more localized dose to the target tissue region.

For example, brachytherapy is performed by implanting radiation sources directly into the tissue to be treated. Brachytherapy is most appropriate where 1) malignant tumor regrowth occurs locally, within 2 or 3 cm of the original boundary of the primary tumor site; 2) radiation therapy is a proven treatment for controlling the growth of the malignant tumor; and 3) there is a radiation dose-response relationship for the malignant tumor, but the dose that can be given safely with conventional external beam radiotherapy is limited by the tolerance of normal tissue. In brachytherapy, radiation doses are highest in close proximity to the radiotherapeutic source, providing a high tumor dose while sparing surrounding normal tissue. Interstitial brachytherapy is useful for treating malignant brain and breast tumors, among others.

Interstitial brachytherapy is traditionally carried out using radioactive seeds such as ¹²⁵I seeds. These seeds, however, produce inhomogeneous dose distributions. In order to achieve a minimum prescribed dosage throughout a target region of tissue, high activity seeds must be used, resulting in very high doses being delivered in some regions in proximity to the seed or seeds which can cause radionecrosis in healthy tissue. One attempt to address this problem, at least with respect to limiting dosages to critical organs near the radioactive seed site, has been to provide a shield directly on a portion of the seed or on an applicator that holds the seed to shield the particularly sensitive tissue. (E.g., Nath et al., Development of an ²⁴¹Am Applicator for Intracavitary Irradiation of Gynecologic Cancers, *Intl. J.*

2

Radiation Oncology Biol. Phys., Vol., 14, pp. 969-978.) While this approach may be appropriate for some applications, it may still be overly "hot" for treating proximate tissue on the unshielded side of the seed, while not providing an effective dose on the shielded side of the seed.

Williams U.S. Pat. No. 5,429,582, entitled "Tumor Treatment," describes a method and apparatus for treating tissue surrounding a surgically excised tumor with radioactive emissions to kill any cancer cells that may be present in the tissue surrounding the excised tumor. In order to implement the radioactive emissions, Williams provides a catheter having an inflatable balloon at its distal end that defines a distensible reservoir. Following surgical removal of a tumor, the surgeon introduces the balloon catheter into the surgically created pocket left following removal of the tumor. The balloon is then inflated by injecting a fluid having one or more radionuclides into the distensible reservoir via a lumen in the catheter.

The apparatus described in Williams solves some of the problems found when using radioactive seeds for interstitial brachytherapy, but leaves some problems unresolved. The absorbed dose rate at a target point exterior to a radioactive source is inversely proportional to the square of the distance between the radiation source and the target point. As a result, where the radioactive source has sufficient activity to deliver a prescribed dose, say 2 centimeters into the target tissue, the tissue directly adjacent the wall of the distensible reservoir, where the distance to the radioactive source is very small, may still be overly "hot" to the point where healthy tissue necrosis may result. In general, the amount of radiation desired by the physician is a certain minimum amount that is delivered to a region up to about two centimeters away from the wall of the excised tumor. It is desirable to keep the radiation that is delivered to the tissue in the target treatment region within a narrow absorbed dose range to prevent over-exposure to tissue at or near the reservoir wall, while still delivering the minimum prescribed dose at the maximum prescribed distance from the reservoir wall. It is also desirable, at least in some applications, to provide these advantages while tailoring the radiation dosage to avoid fully dosing sensitive tissue or to reduce the amount of radiation that escapes the patient's body.

There is still a need for an instrument which can be used to deliver radiation from a radioactive source to target tissue within the human body with a desired intensity and at a predetermined distance from the radiation source without over-exposure of body tissues disposed between the radiation source and the target, and with the ability to shape the radiation dose to protect sensitive tissue or to protect against radiation exposure outside of the patient's body which may affect healthcare providers or others who might come close to the patient.

SUMMARY OF THE INVENTION

The present invention solves the problems described above by providing an interstitial brachytherapy apparatus for delivering radioactive emissions in an asymmetric fashion to target tissue surrounding a surgical extraction site. The apparatus includes an expandable outer surface element defining an apparatus spatial volume, a radiation source disposed within the apparatus volume, and a means for providing predetermined asymmetric isodose profile within the target tissue.

In one configuration, asymmetric isodose curves are created in the target tissue by shaping or locating the radiation source so as to be asymmetrically placed with respect to a

3

longitudinal axis of the apparatus. In one example of an apparatus having this configuration, an inner volume containing a liquid radioisotope is asymmetrically placed within the apparatus volume so as to result in an isodose profile in the target tissue that is asymmetric about the longitudinal axis of the apparatus.

In another example, the radiation source comprises a plurality of spaced apart solid radioactive particles disposed within the apparatus volume and arranged to provide a predetermined asymmetric isodose curve within the target tissue. In one particular example, the plurality of spaced apart radioactive particles are provided on a single elongate member that is shaped so that some of the radioactive particles are farther from the longitudinal axis of the apparatus than others. In other particular examples, a plurality of members carrying radioactive particles are provided with at least one of the members being shaped so as to place at least one radioactive particle asymmetrically with respect to the longitudinal axis of the apparatus.

An interstitial brachytherapy apparatus of the invention may also be implemented in a device having an expandable outer surface defining an apparatus volume, a radiation source disposed within and spaced apart from the expandable outer surface, and at least one asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shielding resulting in predetermined asymmetric isodose curves within the target tissue. In one embodiment, radiopaque shielding is provided on a portion of the expandable outer surface. In another embodiment, the radiation source is encompassed within a second, inner surface within the apparatus volume, with radiopaque shielding provided on at least a portion of the inner surface. In still further embodiments, one or more radiation shields are spaced apart from the radiation source and within the apparatus volume to achieve the desired asymmetric isodose distribution within the target tissue.

The invention also provides a method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location. The method includes surgically creating access to the proliferating tissue within a patient and surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue. An interstitial brachytherapy apparatus for delivering radioactive emissions as described above is then provided and intra-operatively placed into the resection cavity. After a prescribed absorbed dose has been delivered to tissue surrounding the apparatus, the apparatus is removed. The radioactive source material may be placed into the interstitial brachytherapy apparatus after the apparatus is placed in the resection cavity, and may be removed before the apparatus is removed. The method has particular applications to brain and breast cancers.

DESCRIPTION OF THE DRAWINGS

The foregoing features, objects and advantages of the invention will become apparent to those skilled in the art from the following detailed description of a preferred embodiment, especially when considered in conjunction with the accompanying drawings in which:

FIG. 1 is a side view of an interstitial brachytherapy apparatus of the invention for delivering asymmetric radioactive doses to body tissue;

FIG. 2 is a cross-sectional view taken along the line 2—2 in FIG. 1;

FIG. 3 is a side view of an additional embodiment of an interstitial brachytherapy apparatus of the invention;

4

FIG. **3A** is an end view of the interstitial brachytherapy apparatus of FIG. **3**;

FIG. **4** is a side view of an additional embodiment of an interstitial brachytherapy apparatus of the invention;

FIG. **5** is a side view of an interstitial brachytherapy apparatus of the invention configured for use with a liquid radiation source.

FIG. **6** is a side view of an interstitial brachytherapy device of the invention employing radiopaque coatings;

FIG. **7** is a side view of an interstitial brachytherapy device of the invention employing radiopaque coating and a liquid radiation source; and

FIGS. **8** and **9** are end views of interstitial brachytherapy devices of the invention employing radiopaque shields.

DESCRIPTION OF THE PREFERRED EMBODIMENT

A surgical instrument **10** for providing radiation treatment to proliferative tissue in a living patient is illustrated in FIG.

20 1. Surgical instrument **10** includes a tubular body member **12** having first and second lumens **14** and **16** (FIG. **2**) extending from proximal ports **18** and **20** in a molded hub **22**. The first lumen **14** carries a radioactive source **24** and second lumen **16** communicates with inflation port **26** formed through the side wall of the tube **12**.

Affixed to the tubular body **12** proximate the distal end **28** thereof is an outer spatial volume **30** defined by an outer polymeric film barrier **32** that is appropriately spaced from the radioactive source **24**. Outer volume **30** encompasses inflation port **26**. With no limitation intended, the distensible polymeric film walls may comprise a biocompatible, radiation resistant polymer, such as silastic rubbers, polyurethanes, polyethylene, polypropylene, polyester, or PVC. The outer spatial volume **30** may be filled with air, saline or, alternatively, a radiation absorbing fluid, such as a contrast media used in angiography. Alternatively, the surface of outer volume **30** need not be a solid material. For example the surface of the outer volume **30** could be an

30 expandable cage formed from a shape memory metal, such as nitinol, or a suitable plastic, such as an expandable polyethylene cage. Such a cage can be formed in the desired shape to conform to a particular isodose profile, contracted for delivery to the target site in vivo, then expanded to cause **40** the tissue surrounding the surgically resected region to take the appropriate shape. The size of the outer spatial volume **30** generally will correspond approximately to the amount of tissue resected. For some applications, the size of the outer spatial volume **30** may be slightly smaller than the resected **45** volume while for other applications, the outer spatial volume will be slightly larger than the resected volume, allowing the expandable surface of the outer spatial volume to urge tissue on the surface of the resected region into the appropriate shape to promote an even dose distribution **50** around the outer spatial volume in the target tissue. In typical applications, the outer spatial volume has a diameter of approximately 2 to 6 centimeters.

Radiation source **24** comprises a wire **34** having one or more solid radioactive particles **36** located on the wire **34**. **60** For example, radioactive micro spheres of the type available from the 3M Company of St. Paul, Minn., may be used as the solid radioactive particles. Such a solid radioactive particle configuration offers an advantage in that it allows a wider range of radionuclides than if one is limited to liquids. **65** Solid radionuclides that could be used with the delivery device of the present invention are currently generally available as brachytherapy radiation sources. Examples of

radioactive materials which can be selected by a person of ordinary skills in the art for use with the present invention may be found in Tables 1 to 4 of PCT Publication WO 97/19723, which is hereby incorporated by reference.

The, radioactive source 24 can either be preloaded into the catheter at the time of manufacture, or loaded into the device after it has been implanted into the space formerly occupied by the excised tumor. If loaded after implantation, the solid radiation emitting material 36 can be inserted through lumen 14 on a wire 34, for example using an afterloader (not shown).

Radiation source 24 has an asymmetric configuration with respect to a longitudinal axis 38 of the instrument 10. That is, radiation source 24 is shaped so as to result in an isodose profile 40 that varies radially about the longitudinal axis 38. More simply, the isodose profile 40 of FIG. 1 has a shorter radius from the longitudinal axis 38 on the top side of the instrument 10 as shown in FIG. 1 than on the bottom side. The asymmetrically shaped isodose curve 40 may be created by providing a plurality of solid radioactive particles 36 on a curved wire 34 in a spaced apart relationship. This configuration will result in certain of the solid radioactive particles 36 being farther from the longitudinal axis 38 of the instrument 10 than others, and will result in the illustrated asymmetric isodose profile 40. One way to provide the illustrated radioactive source 24 configuration is to form wire 34 from a solid or tubular shape memory alloy such as nickel-titanium alloys known in the art to have such properties. Wire 34 can then be preformed to the desired shape, can be compressed into a substantially straight configuration to pass through lumen 14, and will resume its desired shape once inside volume 30 where wire 34 will be free from steric constraints imposed inside the lumen 14. The resulting asymmetric isodose curve 40 can be further tailored by using solid radioactive particles 36 having differing specific activities to achieve the desired dosing.

In one embodiment, volume 30 and barrier 32 act to separate target tissue from the radiation source 24. Ideally, radiation therapy should make use the inherent difference in radiosensitivity between the tumor and the adjacent normal tissues to destroy cancerous tissue while causing minimal disruption to surrounding normal tissues. At high doses of radiation, however, the percentage of exposed cells that survive treatment decreases with first-order kinetics in proportion to increasing radiation dose. With increasing cell death comes increasing risk of necrosis or tissue death in healthy tissue that is treated with a high dose of radiation. Accordingly, it is desirable to keep the maximum radiation dose delivered by the brachytherapy apparatus as low as possible while still delivering the desired therapeutic dose to the desired range of tissue. One method for achieving this result is to provide a "hotter" radiation source in a spaced apart relationship to the target tissue. In this way, because the intensity of the radiation emitted by a source drops with the square of the distance from the source, the effective dosage may be maintained below necrosis levels in target tissue closest to the interstitial brachytherapy apparatus while providing the required dosage to a greater depth into the target tissue. (See, e.g., U.S. Pat. No. 5,913,813 which is hereby incorporated by reference in its entirety.) The capability of the apparatus of the invention to deliver absorbed doses deeper into the target tissue than prior interstitial brachytherapy devices while controlling the dose in proximity to the apparatus to reduce or eliminate the risk of healthy tissue necrosis allows for the use of brachytherapy in a greater number of cases.

For example, it is desirable to provide an interstitial brachytherapy device configured to provide a dose in a

therapeutic range, say between 40 to 60 Gray, at a distance between 0.5 and 1.0 cm from the outer spatial volume for an outer spatial volume having a diameter of 4.0 cm and being in contact with the resection cavity wall. In a typical embodiment, the radioactive source material ranges from approximately 150 to 450 mCi in activity and encompasses most of the target treatment area with a 0.4 to 0.6 Gray/hour isodose contour. At this treatment rate, treatment may be completed in approximately 3 to 7 days, or more commonly, 10 in approximately 3 to 5 days.

In some applications, the desired dosing profile is consistent with the shape of the outer volume 30. That is, the absorbed dose within the target tissue at points equidistant from the surface 32 of the outer spatial volume 30 should be 15 substantially uniform in substantially every direction. Put another way, the three dimensional isodose profiles generated by the radiation source should be substantially similar in shape to the outer spatial volume 30. Where the apparatus of the invention is deployed in soft tissue, it may also be 20 important for the surface 32 of the outer spatial volume 30 to be sufficiently firm so as to force the target tissue to take on the shape of the surface 30 so that the desired relationship between the isodose profiles and the target tissue is achieved

While the interstitial brachytherapy device 10 of FIG. 1 25 may employ these techniques to positive effect, this device specifically alters the isodose profile for applications where particularly sensitive tissue or other concerns result in a desire to limit the dosage on one or more sides of the device as illustrated by isodose curve 40.

In a further embodiment of the brachytherapy device 50 30 of the invention, illustrated in FIG. 3, three solid radiation particles 52 are provided in a linear portion 54 of radiation source 56, while two additional radiation particles 52 are provided on co-planar extending portions 58, 60 of radiation 35 source 56. An end view of the device 50 of FIG. 3 is shown in FIG. 3A with extending portions 58, 60 provided in a single plane 62, and resulting in isodose profile 64. A second inner, expandable surface 66 can also be provided within outer surface 68; the inner surface 66 enclosing the entirety 40 of radiation source 56.

By providing extending portions 58, 60 having radioactive particles in the indicated co-planar relationship, areas of reduced dosage can be created on opposed sides of the device while maintaining symmetric dosing in all other directions. Of course, the number of sources and their configuration can be changed to create a desired asymmetric dosage. For example, an additional source could be added, for example above plane 62, to result in a symmetric isodose 45 profile in all directions except the direction below the plane 62 which would have a lower dosage.

An additional device 80 of the invention, shown in FIG. 4, includes a radiation source 82 that is made up of three wires 84, 86, 88, each having a plurality of solid radiation 50 particles. Wire 86 is a straight wire extending along the longitudinal axis 90 of the device, while wires 84, 88 each curve as wire 34 described above with respect to FIG. 1. Wires 84, 88 are coplanar, resulting in an isodose profile 92 that is similar to isodose profile 64 of FIG. 3A. That is, the 55 isodose profile will be symmetric in the plane in which the wires 84, 88 are disposed, but will have areas of reduced dosage in directions transverse to that plane (i.e., in FIG. 4, in the directions into and out of the page). As with the device 50 of FIGS. 3 and 3A, device 80 can be configured with 60 more or fewer wires 84, 86, 88, and can be provided in configurations other than the depicted co-planar configuration in order to achieve desired asymmetric isodose profiles.

The asymmetric dosing effect achieved by the devices described above can also be achieved using a liquid radiation source. For example, device 100, illustrated in FIG. 5, has an outer surface 102 defining an outer volume 104 and an inner surface 106 defining an inner volume 108. The inner surface 106 is asymmetrically shaped or located with respect to the longitudinal axis 110 of the device 100 so as to result in the desired asymmetric dosing when the inner volume 108 is filled with a radioactive fluid. The inner volume 108 is spaced apart from the outer surface 102 and can be filled with a material containing a predetermined radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides that emit photons, beta particles, gamma radiation, or other therapeutic rays. The radioactive material contained within the inner volume 108 can be a fluid made from any solution of radionuclide(s), e.g., a solution of Ir-192, I-125 or I-131. A radioactive fluid can also be produced using a slurry of a suitable fluid containing small particles of solid radionuclides, such as Au-198, Y-90. Moreover, the radionuclide(s) can be embodied in a gel. One radioactive material useful in the invention is lotrex™, a sterile single use, non-pyrogenic solution containing sodium 3-(¹²⁵I)iodo-4-hydroxybenzenesulfonate (¹²⁵I-HIBS), available from Proxima Therapeutics, Inc. of Alpharetta, Ga. The inner volume 108 may be filled with radioactive fluid through port 112. Similarly, outer volume 104 can be filled on inflated using port 114.

A desired asymmetric dosing profile having the dosing characteristics described above may also be created by using asymmetric shielding between the radiation source and the target tissue as illustrated in FIGS. 6 through 9. In the device 120 of FIG. 6, a balloon 122 is located on the distal end of catheter 124. Radioactive particles 126 are disposed along the longitudinal axis 128 of the device. A portion of the surface, either inner or outer, of balloon 122 is coated with a radiopaque material 130 to result in asymmetric isodose curve 132. Radiopaque materials suitable for coating onto a polymeric surface of balloon 122 include, for example, barium, tungsten, bismuth, tantalum and tin.

A further device 140 having radiopaque shielding 142 is illustrated in FIG. 7. Device 140 includes an outer volume surface 144 and an inner volume surface 146. Inner surface 146 may contain a liquid radiation source, or may enclose one or more solid particles as used in device 120 (FIG. 6). In device 140, the radiopaque material 142 is coated onto a portion of either the inner or outer side of the inner volume surface 146, resulting in a desired asymmetric isodose profile 148.

Additional devices 160, 180 of the invention having radiation shielding 162 are illustrated in FIGS. 8 and 9, respectively. In these devices 160, 180, one or more radiation shields 162 are provided between and spaced apart from a radiation source (not shown) located along a longitudinal axis 164 of the device and the target tissue, which will be located outside of expandable surface 166. The radiation source can include a liquid or a solid radiation source as described above. Shields 162 can be formed from radiopaque materials including those described above with respect to the radiopaque coating and can extend longitudinally from a base on the device located within the expandable surface 166.

As shown in FIG. 8, device 160 has two radiation shields 162 on opposed sides of catheter 168. This configuration results in lower radiation dosing on the two sides of the device 160 on which the shields 162 are located as shown by isodose curve 170. Device 180 (FIG. 9) has a single radiation shield 162 resulting in an asymmetric isodose curve 182

as shown. A person or ordinary skill in the art will recognize that other configurations may be employed to achieve desired isodose curves.

The interstitial brachytherapy apparatus of the invention can be used in the treatment of a variety of malignant tumors, and is especially useful for in the treatment of brain and breast tumors.

Many breast cancer patients are candidates for breast conservation surgery, also known as lumpectomy, a procedure that is generally performed on early stage, smaller tumors. Breast conservation surgery is typically followed by postoperative radiation therapy. Studies report that 80% of breast cancer recurrences after conservation surgery occur near the original tumor site, strongly suggesting that a tumor bed "boost" of local radiation to administer a strong direct dose may be effective in killing any remaining cancer and preventing recurrence at the original site. The apparatus described herein can be used for either the primary or boost therapy. Numerous studies and clinical trials have established equivalence of survival for appropriate patients treated with conservation surgery plus radiation therapy compared to mastectomy.

Surgery and radiation therapy are also the standard treatments for malignant solid brain tumors. The goal of surgery is to remove as much of the tumor as possible without damaging vital brain tissue. The ability to remove the entire malignant tumor is limited by its tendency to infiltrate adjacent normal tissue. Partial removal reduces the amount of tumor to be treated by radiation therapy and, under some circumstances, helps to relieve symptoms by reducing pressure on the brain.

A method according to the invention for treating these and other malignancies begins by surgical resection of a tumor site to remove at least a portion of the cancerous tumor and create a resection cavity. Following tumor resection, but prior to closing the surgical site, the surgeon intra-operatively places an interstitial brachytherapy catheter apparatus, having an inner spatial volume and an outer spatial volume as described above but without having the radioactive source material loaded, into the tumor resection cavity. Once the patient has sufficiently recovered from the surgery, the interstitial brachytherapy catheter is loaded with a radiation source. The radioactive source dwells in the catheter until the prescribed dose of radiotherapy is delivered, typically for approximately a week or less. The radiation source is then retrieved and the catheter is removed. The radiation treatment may end upon removal of the brachytherapy apparatus, or the brachytherapy may be supplemented by further doses of radiation supplied externally.

It will be understood that the foregoing is only illustrative of the principles of the invention, and that various modifications can be made by those skilled in the art without departing from the scope and spirit of the invention, including, but not limited to, combinations of elements from different embodiments found herein. All references cited herein are expressly incorporated by reference in their entirety.

What is claimed is:

1. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:
an expandable outer surface defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

9

a radiation source disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume, the radiation source further being asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves with respect to the apparatus volume.

5

2. A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of solid radiation sources being provided in a spaced apart relationship on a single elongate member, the single elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources with respect to a longitudinal axis through the apparatus volume.

3. The apparatus of claim 2, further comprising a catheter in communication with the apparatus volume, the elongate member extending through the catheter into the apparatus volume.

4. The apparatus of claim 3, wherein the elongate member is formed of a shape memory alloy, the elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources, taking on a substantially straight shape while being inserted through the catheter to the apparatus volume, and resuming an asymmetric shape when extended into the apparatus volume.

5. A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, wherein at least one of the plurality of solid radiation sources has a different specific activity from at least one other solid radiation source.

6. A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source compris-

10

ing a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of radiation sources being provided on at least two elongate members extending into the apparatus volume, at least one of the elongate members being shaped to provide asymmetric placement of a radiation source with respect to a longitudinal axis through the apparatus volume.

10 7. The apparatus of claim 6, wherein each of the at least two elongate members includes a plurality of solid radiation sources provided in a spaced apart relationship.

8. The apparatus of claim 1, wherein the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth.

9. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

20 an expandable outer surface having a base and defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

a radiation source disposed completely within and spaced apart from the expandable outer surface; and

30 an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with respect to the apparatus volume.

10. The apparatus of claim 9, wherein the asymmetric radiation shield comprises a radio-opaque material disposed on only a portion of the expandable outer surface.

11. The apparatus of claim 10, wherein the expandable outer surface comprises an inflatable balloon.

12. The apparatus of claim 11, wherein the radiation shield comprises a barium material disposed a portion of the inflatable balloon.

13. The apparatus of claim 9, further comprising at least one radiation shield extending from the base of the expandable outer surface toward an opposite end of the expandable surface, the shield being in between and spaced apart from the radiation source and the expandable outer surface, the shield forming a radio-opaque barrier between a portion of the radiation source and the target tissue.

40 45 14. The apparatus of claim 13, wherein the radiation shield comprises two shields provided on opposite sides of the radiation source.

* * * * *

EXHIBIT D

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CYTYC SURGICAL PRODUCTS II, INC.

7

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

11 XOFT, INC.,) Case No. CV 05-05312 RMW
12 Plaintiff,)
13 vs.)
14 CYTYC CORPORATION and PROXIMA)
THERAPEUTICS, INC.,)
15 Defendants.)
16) Tutorial and Markman Hearing
17 AND RELATED COUNTERCLAIMS.) Date: December 20, 2006
18) Time: To Be Set
) Room: Courtroom 6, 4th Floor
) Judge: Hon. Ronald M. Whyte
)
)

HOWREY LLP

TABLE OF CONTENTS

	<u>Page</u>
PRELIMINARY STATEMENT	1
BACKGROUND	2
I. THE TECHNOLOGY	2
II. THE EXPERTS	3
APPLICABLE LAW	4
CONSTRUCTION OF CLAIM TERMS	7
I. TERMS IN THE '813 PATENT	7
A. "Inner Spatial Volume" (All Asserted Claims)	8
B. "Outer, Closed, Inflatable Chamber" (All Asserted Claims)	9
C. "Predetermined Constant Spacing" (All Asserted Claims)	10
D. "Predetermined Constant Spacing Between Said Inner Spatial Volume And The Radiation Transparent Wall" (All Asserted Claims)	11
E. "Rendering Uniform" (All Asserted Claims)	11
F. "Means . . . For Rendering Uniform The Radial Absorbed Dose Profile Of The Emissions" (All Asserted Claims)	12
G. "The Radioactive Material" (Claim 8)	14
H. "A Plurality Of Radioactive Solid Particles Placed At Pre-determined Locations Within The Inner Spatial Volume To Provide A Desired Composite Radiation Profile" (Claim 12)	15
II. TERMS IN THE '204 PATENT	15
A. "Interstitial" (All Asserted Claims)	16
B. "Brachytherapy" (All Asserted Claims)	16
C. "Interstitial Brachytherapy" (All Asserted Claims)	17
D. "Inner Spatial Volume" (All Asserted Claims)	18
E. "Outer Spatial Volume" (All Asserted Claims)	19
F. "Expandable Surface Element" (All Asserted Claims)	20
G. "Radiation Source" (All Asserted Claims)	20
H. "Minimum Prescribed Dose" (Claims 2, 18, 24, 32, & 36)	21

1	I.	"Delivering A Prescribed Absorbed Dose" (Claim 34).....	21
2	J.	"The Inner And Outer Spatial Volumes Are Configured To Provide A Minimum Prescribed Absorbed Dose" (Claim 2 & 36) And "Configuring The Inner And Outer Spatial Volumes To Provide A Minimum Prescribed Absorbed Dose" (Claims 24 & 32)	22
3	K.	"A Minimum Distance Outward From The Outer Spatial Volume Expandable Surface" (Claims 2, 24, 32, & 36).....	23
4	L.	"Controlled Dose" (Claim 2, 24, 32, & 36)	23
5	M.	"To Reduce Or Prevent Necrosis In Healthy Tissue Proximate To The Expandable Surface" (Claims 2, 24, 32, & 36).....	24
6	N.	"Providing A Controlled Dose At The Outer Spatial Volume Expandable Surface To Reduce Or Prevent Necrosis In Healthy Tissue" (Claims 2, 24, 32 & 36)	24
7	O.	"Adapting The Expandable Surface To Contact Tissue Surrounding The Resection Cavity To Conform The Tissue" (Claim 34)	25
8	P.	"Desired Shape Of The Expandable Surface Element" (Claims 4, 26, & 34).....	26
9	Q.	"Predetermined Spacing" (Claims 3 & 25).....	26
10	R.	"A Predetermined Spacing Is Provided Between Said Inner Spatial Volume And The Expandable Surface Element"/ "A Predetermined Spacing Between Said Inner Spatial Volume And The Expandable Surface Element" (Claims 3 & 25)	27
11	S.	"Intraoperatively" (Claims 19 & 34)	28
12	T.	"Solid Radiation Source" (Claim 16)	28
13	U.	"The Prescribed Absorbed Dose Is Delivered To The Target Tissue In Substantially Three Dimensions" (Claim 18)	28
14	CONCLUSION		29
15			
16			
17			
18			
19			
20			
21			
22			
23			
24			
25			
26			
27			
28			

TABLE OF AUTHORITIES

Page

CASES

4	<i>ACTV, Inc. v. Walt Disney Co.</i> , 346 F.3d 1082 (Fed. Cir. 2003)	10
5	<i>Bancorp Servs., LLC v. Hartford Life Ins. Co.</i> , 359 F.3d 1367 (Fed. Cir. 2004)	7
6	<i>BBA Nonwovens Simpsonville, Inc. v. Superior Nonwovens, L.L.C.</i> , 303 F.3d 1332 (Fed. Cir. 2002)	12
7	<i>Epcon Gas Sys., Inc. v. Bauer Compressors, Inc.</i> , 279 F.3d 1022 (Fed. Cir. 2002)	6
8	<i>Exxon Research & Eng'g Co. v. United States</i> , 265 F.3d 1371 (Fed. Cir. 2001)	6
9	<i>Fresenius Med. Care Holdings, Inc. v. Baxter Int'l, Inc.</i> , No. C 03-1431 SBA, 2006 U.S. Dist. LEXIS 36788 (N.D. Cal. May 24, 2006)	7
10	<i>Greenberg v. Ethicon Endo-Surgery, Inc.</i> , 91 F.3d 1580 (Fed. Cir. 1996)	6
11	<i>Hybritech Inc. v. Monoclonal Antibodies, Inc.</i> , 802 F.2d 1367 (Fed. Cir. 1986)	7
12	<i>In re Am. Acad. of Sci. Tech. Ctr.</i> , 367 F.3d 1359 (Fed. Cir. 2004)	5
13	<i>Intel Corp. v. VIA Techs.</i> , 319 F.3d 1357 (Fed. Cir. 2003)	7
14	<i>Kahn v. General Motors Corp.</i> , 135 F.3d 1472 (Fed. Cir. 1998)	6, 14
15	<i>Miles Labs., Inc. v. Shandon, Inc.</i> , 997 F.2d 870 (Fed. Cir. 1993)	6
16	<i>Pfizer, Inc. v. Teva Pharm.USA, Inc.</i> , 429 F.3d 1364 (Fed. Cir. 2005)	14
17	<i>Phillips v. AWH Corp.</i> , 415 F.3d 1303 (Fed. Cir. 2005) (en banc), <i>cert. denied</i> , 126 S. Ct. 1332 (2006)	passim
18	<i>S3 Inc. v. nVidia Corp.</i> , 259 F.3d 1364 (Fed. Cir. 2001)	27
19	<i>SanDisk Corp. v. Memorex Prods., Inc.</i> , 415 F.3d 1278 (Fed. Cir. 2005)	14

1	<i>Vitronics Corp. v. Conceptronic, Inc.</i> , 90 F.3d 1576 (Fed. Cir. 1996)	14
2	STATUTES	
3	35 U.S.C.A. § 112, ¶ 6 (West 2001).....	6, 12

STATUTES

1 Pursuant to the Agreed Scheduling Order,¹ Defendant and Counterclaimant Cytac Corporation
 2 (“Cytac”) respectfully submits this Brief addressing the construction of disputed terms, phrases and
 3 clauses in the asserted claims of U.S. Patent Nos. 5,913,813 (the “‘813 patent”) and 6,413,204 (the
 4 “‘204 patent”) (attached hereto as Exhibits A and B to the Declaration of Henry C. Su, respectively).
 5 Cytac currently asserts claims 1, 2, 3, 4, 8 and 12 of the ‘813 patent and claims 1, 2, 3, 4, 8, 16, 17, 18,
 6 19, 20, 21, 23, 24, 25, 26, 30, 32, 34, 35 and 36 of the ‘204 patent against Plaintiff Xoft, Inc. (“Xoft”).

7 **PRELIMINARY STATEMENT**

8 The differences in the parties’ approaches to construing the disputed terms are stark. Cytac’s
 9 proposed constructions are straightforward, applying the plain meaning that would be apparent to one
 10 of ordinary skill in the art when the disputed terms are read in light of the specification, in accordance
 11 with the Federal Circuit’s recent *en banc* decision in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir.
 12 2005) (*en banc*), *cert. denied*, 126 S. Ct. 1332 (2006). In contrast, Xoft insists on improperly injecting
 13 into its proposed constructions of the disputed terms limitations that are nowhere found in the claim
 14 language and are not supported by the specification, in contravention of Federal Circuit law. Xoft also
 15 repeatedly attempts to limit the claim terms to exemplary embodiments in the specification, which is
 16 also contrary to the law. In a few instances where the patent specifically defines a claim term, Xoft
 17 refuses to acknowledge that express definition, crafting instead its own definition from whole cloth.
 18 Finally, Xoft cannot hope to establish by clear and convincing evidence that certain claims terms are
 19 indefinite. The testimony of Cytac’s expert, Dr. Lynn J. Verhey, shows that one skilled in the art,
 20 reading the disputed terms in light of the specification, understands exactly what is being claimed.
 21 Xoft’s strained interpretations of the disputed terms and its meritless allegations of indefiniteness
 22 should thus be rejected.

23

24 ¹ The Agreed Scheduling Order called for Cytac to file its Opening Claim Construction Brief on November 6, 2006. On
 25 account of the fact that the Court was moving the date for the technology tutorial and claim construction hearing from
 26 December 6-7, 2006 to December 20, 2006, the parties filed on November 3, 2006 a joint stipulation and proposed order
 27 requesting that the Court enlarge the briefing schedule. On November 7, 2006, the Court declined to enlarge the briefing
 28 schedule (other than to set the due date for the reply brief on December 7, 2006) and held that “[h]aving at least the
 minimum time periods set forth in Civil L.R. 7 to consider the parties’ arguments would be particularly useful to the court
 in a case such as this.” In response to this order, Cytac moved promptly to finalize and file its Opening Claim Construction
 Brief, which is still being submitted more than 35 days before the scheduled hearing date.

BACKGROUND

I. THE TECHNOLOGY

The patents-in-suit relate to the field of treating proliferative tissue diseases like cancer with radiation. Traditionally, a patient diagnosed with a cancerous tumor would have the tumor removed and then the region of body where the tumor was located would be exposed to an external radiation beam in an attempt to ensure that any remaining cancerous cells are destroyed. One of the major disadvantages of external beam radiation therapy is that it is difficult to target just the diseased area and avoid irradiating significant portions of healthy tissue. Accordingly, it is medically desirable to use various devices and instruments to position the radiation source as close as possible to the diseased site. This technique is known as brachytherapy. The root “brachy” comes from the Greek word for “short distance.”

12 The patents-in-suit are directed specifically to a type of brachytherapy known as interstitial
13 brachytherapy, in which the radiation source is introduced in close proximity to diseased cells that are
14 within the interstices of a body tissue. This technique requires creating some sort of path through the
15 tissue to the reach the targeted site, and it can be contrasted with brachytherapy in which the radiation
16 source is merely inserted into a natural body cavity like the bladder (intracavitory), into a body lumen
17 like the urethra (intraluminal), or on the surface of the body (surface brachytherapy). For example, as
18 taught by the patents-in-suit, a radiation source is introduced through the opening and cavity created by
19 the tumor resection so that it can treat the diseased cells within the interstices of the tissue at the
20 margins of the tumor resection site.

According to the invention described and claimed in the patents-in-suit, the radiation source is introduced into the resection cavity using a catheter. An expandable or inflatable device, such as a cage or balloon, is used to shape the resection cavity so that the radiation dose absorbed by the diseased cells within the interstices of the tissue at the margins of the cavity is made more uniform. Three primary factors affect the amount of the absorbed dose: (1) distance of the tissue to be treated from the radiation source, (2) the presence of a radiation attenuating medium such as air or a saline solution, and (3) the use of radiation shielding.

1 The patents-in-suit use these factors, individually or in combination, to improve treatment by
 2 controlling the “radial absorbed dose profile” and the “three-dimensional isodose profile.” The former
 3 involves controlling the absorbed dose as a function of radial distance from the radiation source to
 4 points within the targeted tissue; the latter involves conforming the shape of the targeted tissue to a
 5 virtual, three-dimensional surface defined by points receiving the same radiation dose. To control the
 6 radial absorbed dose profile, one may surround the radiation source with a radiation attenuating
 7 medium to minimize the ratio of the absorbed dose at the wall of the tumor cavity to the dose within
 8 the interstices of the target tissue. If the ratio is too high, then “hot spots” can occur at the wall of the
 9 cavity, which cause healthy tissue to necrose. Controlling the three-dimensional isodose profile
 10 involves shaping the resected tumor cavity and adjusting the position of the radiation source relative to
 11 the cavity to create a desired, virtual isodose surface on which all points receive substantially the same
 12 dose. These points will be coincident with points within the interstices of the tissue to be treated.

13 **II. THE EXPERTS**

14 Although Cytac bases its proposed constructions on the intrinsic evidence, *i.e.*, the patents’
 15 claim language, specifications, and prosecution histories, Cytac also proffers the testimony of Dr.
 16 Lynn J. Verhey to provide the perspective of one skilled in the relevant art. *Phillips*, 415 F.3d at 1313
 17 (claims must be construed from the perspective of one skilled in the art). In this case, a person of
 18 ordinary skill in the art has a background in radiation oncology physics with a focus on brachytherapy.
 19 Such individuals would hold a M.S. degree in Physics or Engineering, with 3 or more years of clinical
 20 medical physics experience, or a Ph.D. in Physics or Engineering with 2 or more years of clinical
 21 experience. (*See Exhibit D to the Declaration of Henry C. Su (Declaration of Lynn J. Verhey, Ph.D.*
 22 (“Verhey Rep.”)) at 4:6-18.)

23 Dr. Verhey is an expert in the field of radiation oncology, with decades of experience. He is
 24 currently a Full Professor and Vice-Chair in the Department of Radiation Oncology at University of
 25 California, San Francisco. Dr. Verhey earned a Ph.D. in Physics and, in 1975, took a position as
 26 Hospital Radiation Physicist at Massachusetts General Hospital (MGH) with a concurrent continuing
 27 position as Assistant Professor at the Harvard Medical School. In 1990, he became Chief of the
 28 Physics Division and Associate Professor in the Department of Radiation Oncology at UCSF. He has

1 taught courses in physics, radiation, and medical physics (including radiation oncology). He has
 2 conducted research on new methods of delivering radiation to cancer patients and has published over
 3 100 technical papers in that field. Dr. Verhey is a certified Therapeutic Radiological Physicist by the
 4 American Board of Radiology and is a fellow in the American Association of Physics in Medicine and
 5 the American Society of Therapeutic Radiology and Oncology. In sum, he is a well-recognized and
 6 independent expert in methods of delivering radiation to cancer patients.

7 By contrast, Xoft's expert, Paul A. Lovoi, Ph.D., did not attach a curriculum vitae to his report
 8 and his credentials in the relevant field are not otherwise apparent. Moreover, Dr. Lovoi is not
 9 independent. He is one of the founders of Xoft and was an officer of Xoft until recently. He now
 10 consults for Xoft and has worked for the company during the last decade. His report indicates a Ph.D.
 11 in physics but does not list any specific experience in the field of radiation oncology, other than 9 years
 12 of purported experience in "medical use of sources of radiation." Xoft is Dr. Lovoi's company – he
 13 founded it, he ran it, and he has devoted a good part of his life to it. This Court should weigh his
 14 opinions accordingly.

15 APPLICABLE LAW

16 Sitting *en banc*, the Federal Circuit recently clarified its guiding principles for construction of
 17 patent claims. *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005). In *Phillips*, the court
 18 emphasized the "primary importance" of the language of the claims themselves:

19 It is a "bedrock principle" of patent law that "the claims of a patent define the invention
 20 to which the patentee is entitled the right to exclude." . . . That principle has been
 21 recognized since at least 1836, when Congress first required that the specification
 22 include a portion in which the inventor "shall particularly specify and point out the part,
 23 improvement, or combination, which he claims as his own invention or discovery." . . .
 24 In the following years, the Supreme Court made clear that the claims are "of primary
 25 importance, in the effort to ascertain precisely what it is that is patented." . . . Because
 26 the patentee is required to "define precisely what his invention is," the Court explained,
 27 it is "unjust to the public, as well as an evasion of the law, to construe it in a manner
 28 different from the plain import of its terms." . . .

29 415 F.3d at 1312 (citations omitted). The Federal Circuit also reaffirmed the time-honored rule that
 30 claim terms are generally to be given their ordinary and customary meaning to those skilled in the art:

31 We have frequently stated that the words of a claim "are generally given their ordinary
 32 and customary meaning." . . . We have made clear, moreover, that the ordinary and
 33 customary meaning of a claim term is the meaning that the term would have to a person
 34 of ordinary skill in the art in question at the time of the invention, i.e., as of the effective

1 filing date of the patent application. . . . The inquiry into how a person of ordinary skill
 2 in the art understands a claim term provides an objective baseline from which to begin
 3 claim interpretation.

4 *Id.* at 1312-13 (citations omitted). Likewise, the court stressed that claims must be read in light of the
 5 specification. *Id.* at 1315 (“claims must be read in view of the specification, of which they are a part.”)
 6 (internal quotations omitted)). Importantly, the court held that claim terms should be given “*their*
 7 *broadest reasonable construction* ‘in light of the specification as it would be interpreted by one of
 8 ordinary skill in the art.’” *Id.* at 1316 (citing *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364
 9 (Fed. Cir. 2004) (emphasis added).

10 The *Phillips* court repeated the venerable warning that one must “avoid the danger of reading
 11 limitations from the specification into the claim.” 415 F.3d at 1323. With that warning in mind, the
 12 court described the two primary instances in which the specification can limit the meaning of claim
 13 terms. *First*, the patentee can choose to recite an explicit definition for a claim term in the
 14 specification. *Id.* at 1316. In that case it is said that the patentee has acted as his own lexicographer
 15 and the patentee’s definition “governs.” *Id.* *Second*, the specification may limit the plain meaning of a
 16 claim term when the patentee disclaims or disavows certain interpretations of the term. *Id.* In other
 17 words, the specification can limit the plain meaning of claim terms when the patentee has clearly set
 18 forth a limiting interpretation.

19 The prosecution history is also important to consider when construing claim terms. The
 20 *Phillips* court explained:

21 [W]e have held that a court “should also consider the patent’s prosecution history, if it
 22 is in evidence.” . . . The prosecution history, which we have designated as part of the
 23 “intrinsic evidence,” consists of the complete record of the proceedings before the PTO
 24 and includes the prior art cited during the examination of the patent. . . . Like the
 25 specification, the prosecution history provides evidence of how the PTO and the
 26 inventor understood the patent. . . . Furthermore, like the specification, the prosecution
 27 history was created by the patentee in attempting to explain and obtain the patent.
 28

415 F.3d at 1317 (citations omitted).

29 The *Phillips* court also noted that expert testimony (on which Xoft almost exclusively relies in
 30 this case) should play a lesser role in claim construction. 415 F.3d at 1317 (“[W]hile extrinsic
 31 evidence ‘can shed useful light on the relevant art,’ we have explained that it is ‘less significant than
 32

1 the intrinsic record in determining the legally operative meaning of claim language.””) (internal
 2 quotations omitted). The court added that:

3 extrinsic evidence in the form of expert testimony can be useful to a court for a variety
 4 of purposes, such as to provide background on the technology at issue, to explain how
 5 an invention works, to ensure that the court’s understanding of the technical aspects of
 6 the patent is consistent with that of a person of skill in the art, or to establish that a
 7 particular term in the patent or the prior art has a particular meaning in the pertinent
 8 field. . . . However, conclusory, unsupported assertions by experts as to the definition
 9 of a claim term are not useful to a court. Similarly, *a court should discount any expert
 10 testimony “that is clearly at odds with the claim construction mandated by the claims
 11 themselves, the written description, and the prosecution history, in other words, with the
 12 written record of the patent.”*

13 *Id.* at 1318 (emphasis added; citations omitted).

14 One claim limitation from the ‘813 patent uses the term “means,” which creates a presumption
 15 that the limitation is drafted in “means plus function” format pursuant to 35 U.S.C. § 112, ¶ 6.
 16 *Greenberg v. Ethicon Endo-Surgery, Inc.*, 91 F.3d 1580, 1584 (Fed. Cir. 1996). “Construction of a
 17 means plus function limitation requires identification of the function recited in the claim and a
 18 determination of what structures have been disclosed in the specification that correspond to the means
 19 for performing that function.” *Epcon Gas Sys., Inc. v. Bauer Compressors, Inc.*, 279 F.3d 1022, 1032
 20 (Fed. Cir. 2002). Structure described in the specification constitutes “corresponding structure” if the
 21 specification “clearly links or associates that structure to the function recited in the claim.” *Kahn v.*
 22 *General Motors Corp.*, 135 F.3d 1472, 1476 (Fed. Cir. 1998).

23 The Federal Circuit has held that a claim must be “definite” enough to be understood by one
 24 skilled in the art:

25 We have stated the standard for assessing whether a patent claim is sufficiently definite
 26 to satisfy the statutory requirement as follows: If one skilled in the art would understand
 27 the bounds of the claim when read in light of the specification, then the claim satisfies
 28 section 112 paragraph 2.

29 *Exxon Research & Eng’g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001) (citing *Miles
 30 Labs., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1993)). “If the meaning of the claim is
 31 discernible, even though the task may be formidable and the conclusion may be one over which
 32 reasonable persons will disagree, we have held the claim sufficiently clear to avoid invalidity on
 33 indefiniteness grounds.” *Id.* See also *Fresenius Med. Care Holdings, Inc. v. Baxter Int’l, Inc.*, No. C

1 03-1431 SBA, 2006 U.S. Dist. LEXIS 36788, at *51 (N.D. Cal. May 24, 2006). As the party asserting
 2 invalidity, Xoft bears the burden of proving indefiniteness. Moreover, because patents enjoy a
 3 statutory presumption of validity, Xoft's burden is heightened – it must prove its case with clear and
 4 convincing evidence. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1375
 5 (Fed. Cir. 1986). A claim is not indefinite merely because it poses a difficult issue of claim
 6 construction (which is not even the case here, where construction is straightforward); if the claim can
 7 be construed at all, then it is not invalid for indefiniteness. *See, e.g., Bancorp Servs., LLC v. Hartford*
 8 *Life Ins. Co.*, 359 F.3d 1367, 1371 (Fed. Cir. 2004). Thus, the biased, conclusory statements of Xoft's
 9 expert alone cannot establish indefiniteness by clear and convincing evidence. *See Intel Corp. v. VIA*
 10 *Techs.*, 319 F.3d 1357, 1367 (Fed. Cir. 2003) (expert's conclusory statements are insufficient to
 11 provide clear and convincing evidence of indefiniteness).

12 CONSTRUCTION OF CLAIM TERMS²

13 I. TERMS IN THE '813 PATENT

14 The claims of the '813 patent relate to an instrument comprising a concentric arrangement of an
 15 inner spatial volume and an outer spatial volume defined by an inflatable chamber, disposed near the
 16 distal end of a catheter body. One of the volumes contains a source of radiation, while the other
 17 volume may contain a radiation absorptive material. In one preferred embodiment, shown in Figure 1
 18 of the patent, the inner volume is defined by an enclosed chamber surrounding the catheter body and
 19 containing a radioactive source. The outer chamber, concentric with the inner volume, is then inflated
 20 with air or other radiation absorbing material so that its wall contacts the wall of the surgical cavity
 21 substantially at all points. The distance between the radiation source and the wall of the outer chamber
 22 can be made constant. This embodiment permits the controlled delivery of radiation to a layer of tissue
 23 surrounding the surgical cavity.³ By manipulating the volume and type of material in the outer
 24

25 ² Cytac addresses herein only those terms about which the parties disagree and which Cytac believes to be material to
 26 resolution of this suit. As to terms not addressed, Cytac's position is as set forth in the parties' Joint Claim Construction
 Statement, which Cytac incorporates by reference herein.

27 ³ The tissue to be treated and the resected cavity can be thought of as an orange peel with the fruit (*i.e.*, the tumor)
 28 removed. A radiation source is placed within the space previously occupied by the fruit. The thickness of the "orange
 (Continued...)

1 chamber, the ratio of the absorbed dose at the surface of the wall of tissue to the dose at the tissue
 2 depth where the minimum dose is prescribed to be received can be controlled so as to maximize the
 3 effectiveness of the treatment and minimize adverse side effects, namely, unwanted necrosis of healthy
 4 tissue.

5 The ‘813 patent teaches that other embodiments can be used to deliver therapeutic radiation to
 6 the layer of tissue surrounding the surgical cavity. (Col 2:64 – 4:20; FIGS. 3-5.) These other
 7 embodiments include the use of a radioactive liquid within an inner inflatable chamber, a plurality of
 8 radioactive solid particles, a slurry of a fluid containing particles of a radioactive isotope or a solid
 9 radioactive source. Alternatively, these same radiation sources can be placed in the volume of space
 10 between the inner chamber and the outer inflatable chamber. Any of these embodiments might be used
 11 as a means of delivering radiation to tissue within the wall of a surgical cavity.

12 **A. “Inner Spatial Volume” (All Asserted Claims)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
A region of space surrounded by an outer spatial volume that is defined by a closed inflatable chamber.	Inner balloon in two-balloon device or spherical solid radionuclide in one-balloon device.

17 Xoft’s attempt to limit the “inner spatial volume” to a “balloon” or a “spherical solid
 18 radionuclide” should be rejected. As an initial matter, a “balloon” is not even one of the embodiments
 19 of the “inner spatial volume” described in the specification. Rather, the specification describes, as an
 20 exemplary embodiment, that “the inner spatial volume 30 . . . may be defined by a generally spherical
 21 polymeric film wall 32.” (Col. 2:35-36 (emphasis added).) In any event, it is improper to limit the
 22 claim language to the embodiments in the specification, as Xoft proposes. *Phillips*, 415 F.3d at 1323
 23 (“For instance, although the specification often describes very specific embodiments of the invention,
 24 we have repeatedly warned against confining the claims to those embodiments.”).

25

26

(...Continued)

27

“peel” corresponds to the thickness of the tissue to be treated – in most procedures the “orange peel” of tissue to be treated is about 2 centimeters thick. (See, e.g., ‘813 patent at FIG. 4.)

28

More fundamentally, Xoft confuses the tangible structure that defines the inner spatial volume with the volume itself. The specification provides that the inner spatial volume 30 “may be *defined by* a generally spherical polymeric film.” The film defines the boundary of the volume but the volume is the region of space within that boundary. (Exhibit C to the Declaration of Henry C. Su (American Heritage College Dictionary (“AHC”)) at 1513.) Thus, according to the specification, the inner spatial volume is simply a region of space surrounded by an outer spatial volume. (*See* col. 1:52-55 (“a first spatial volume at the distal end of a catheter and a second spatial volume defined by a surrounding of the first spatial volume by a polymeric film wall . . . ”).)

Cytyc’s proposed construction fully captures the plain meaning of “inner spatial volume,” which the Federal Circuit notes is of “primary importance” in claim construction. *Phillips*, 415 F.3d at 1312. A “spatial volume” is a commonly understood English term, meaning simply “a region of space.” (AHC at 1513.) The word “inner” means that that region of space is located within something else, and the specification provides that that “something else” is another (outer) “spatial volume.” (Col. 1:52-55.) “Inner spatial volume” should therefore be construed to mean “a region of space surrounded by an outer spatial volume that is defined by a closed inflatable chamber.”

B. “Outer, Closed, Inflatable Chamber” (All Asserted Claims)

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Inflatable balloon, i.e., deflated balloon.

Cytyc believes that no construction of this term is required or appropriate. The term has its ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic evidence. There is no evidence of any intent by the inventors to impart a novel or special meaning to the term and Xoft has pointed to none. As discussed above with respect to an “inner spatial volume,” Xoft’s construction improperly attempts to limit the claim term to just a balloon. But nothing in the specification limits the outer, closed inflatable chamber to a “balloon.” Xoft’s proposed construction is not supported by the specification and is contrary to law. Cytyc proposes the term be given its plain meaning: an “outer, closed, inflatable chamber.” Examples of such a chamber include an inflatable balloon or an expandable cage, and as Dr. Verhey points out, an “inflatable chamber of any type”

1 could satisfy this limitation. This, Xoft's proposed construction should be rejected and the plain
2 meaning of the term adopted.

C. “Predetermined Constant Spacing” (All Asserted Claims)

Cytec's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Indefinite. “Predetermined” spacing is some undefined constant spacing predetermined in some undefined manner with regard to deflated outer chamber.

Cytc addresses the construction of this term in connection with its construction of the term “a predetermined constant spacing between said inner spatial volume and the radiation transparent wall” below. Cytc believes that a separate construction of this term divorced from the context of the surrounding claim language is neither required nor appropriate. *See Phillips*, 415 F.2d at 1314 (“Quite apart from the written description and the prosecution history, the claims themselves provide substantial guidance as to the meaning of particular claim terms. . . . To begin with, the context in which a term is used in the asserted claim can be highly instructive.”) (citing *ACTV, Inc. v. Walt Disney Co.*, 346 F.3d 1082, 1088 (Fed. Cir. 2003) (“the context of the surrounding words of the claim also must be considered in determining the ordinary and customary meaning of those terms”)).

Xoft proposes no construction of this term, arguing that it is indefinite. Contrary to Xoft’s assertion, the term “predetermined constant spacing” is not indefinite and has an ordinary and customary meaning to one skilled in the art. Dr. Verhey easily understood the phrase “predetermined constant spacing” – indeed, any speaker of English can understand it – to mean that the spacing between the inner spatial volume and the wall of the outer inflatable chamber is made to be substantially constant. This spacing is “predetermined” in the sense that it is chosen in advance by one skilled in the art. (Exhibit C at 1077.) Although Xoft incorrectly suggests that the patent must describe that amount of spacing, a patent does not need to describe what one skilled in the art already knows. *See S3 Inc. v. nVidia Corp.*, 259 F.3d 1364, 1371 (Fed. Cir. 2001) (“The law is clear that patent documents need not include subject matter that is known in the field of the invention and is in the prior art, for patents are written for persons experienced in the field of the invention. . . . To hold

1 otherwise would require every patent document to include a technical treatise for the unskilled
 2 reader.”) (citation omitted). One skilled in the art knows how to determine an appropriate
 3 “predetermined constant spacing.” Xoft cannot possibly show that the term is indefinite by clear and
 4 convincing evidence.

5 **D. “Predetermined Constant Spacing Between Said Inner Spatial Volume And**
 The Radiation Transparent Wall” (All Asserted Claims)

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
The spacing between the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, can be made constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical.	Indefinite. <i>See</i> “predetermined constant spacing,” <i>supra</i> , § I.C.

12 Xoft proposes no construction of this term, arguing only that it is indefinite. The conclusory
 13 statement of Dr. Lovoi, who works for Xoft and thus cannot provide a neutral opinion, does not come
 14 close to providing the clear and convincing evidence needed for Xoft to show indefiniteness. To the
 15 contrary, the term is readily understood by those skilled in the art. As Dr. Verhey explains, the term
 16 means that the spacing between the inner spatial volume and the radiation transparent wall of the outer,
 17 closed inflatable chamber, when inflated, can be made constant. If the outer chamber is spherical, then
 18 the distance is constant in all directions. If the outer chamber is cylindrical, then the distance is
 19 constant around a radial plane that is perpendicular to the axis of the catheter. (Verhey Rep. at 7:2-5.)
 20 This plain meaning construction should be adopted. *Phillips*, 415 F.3d at 1312 (plain meaning is of
 21 “primary importance”).

22 **E. “Rendering Uniform” (All Asserted Claims)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Making the same, i.e., causing to have the same value or characteristic at all points.

27 Cytyc addresses the construction of this term in connection with its construction of the term
 28 “means . . . for rendering uniform the radial absorbed dose profile of the emissions” below. Cytyc

1 believes that a separate construction of this term divorced from the context of the surrounding claim
2 language is neither required nor appropriate. *See Phillips*, 415 F.3d at 1314.

F. "Means . . . For Rendering Uniform The Radial Absorbed Dose Profile Of The Emissions" (All Asserted Claims)

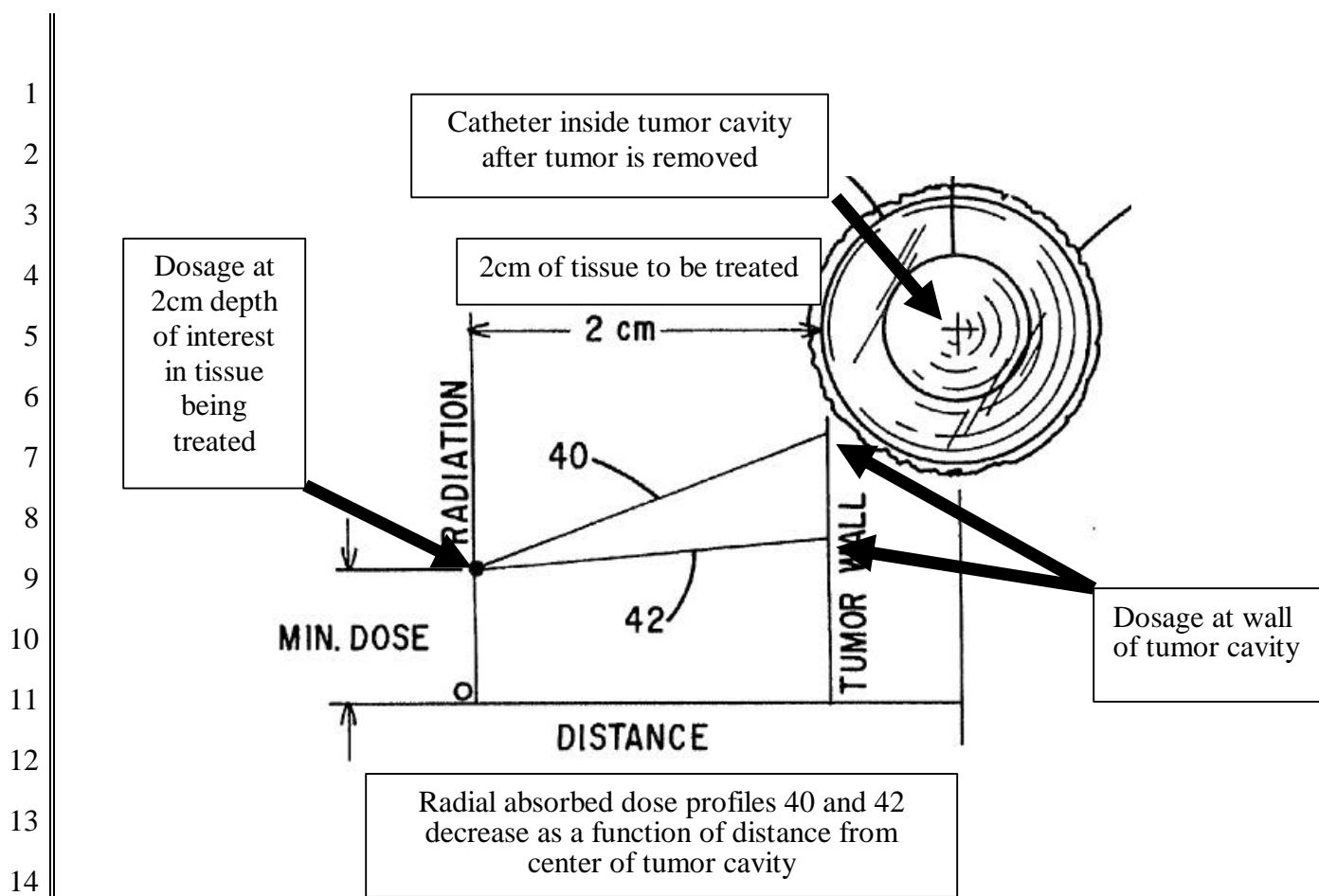
Cytec's Proposed Construction	Xoft's Proposed Construction
<p><i>Disputed Function:</i> Modifying the ratio of the absorbed dose at a depth of interest in the target tissue to the absorbed dose at the surface of the tissue.</p> <p><i>Disputed Structure:</i> A radiation absorbing or attenuating material, e.g., air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfite.</p>	<p><i>Disputed Function:</i> Making the dose along a radius extending from the radionuclide outwardly from the outer chamber wall the same at every point on the radius.</p> <p><i>Disputed Structure:</i> No such means disclosed in the '813 patent, means for making more uniform disclosed as substance within outer chamber.</p>

Because this is a “means-plus-function” limitation subject to 35 U.S.C. § 112, ¶ 6, the Court must construe the limitation’s function as well as the structure disclosed in the specification that corresponds to that function. *BBA Nonwovens Simpsonville, Inc. v. Superior Nonwovens, L.L.C.*, 303 F.3d 1332, 1343 (Fed. Cir. 2002) (Construction of a means-plus-function limitation “requires the court to first identify the function of the means-plus-function limitation and next identify the corresponding structure in the written description necessary to perform that function.”). The function required by this limitation is “rendering uniform the radial absorbed dose profile of the emissions.” As Dr. Verhey explains, the radial absorbed dose profile is defined as the absorbed dose in tissue, varying as a function of distance from the center of the cavity along a particular direction of interest. (Verhey Rep. at 6:21-23.) In the ‘813 patent, the direction of interest would be from the wall of the surgical cavity to a depth in the target tissue at which a prescribed therapeutic dose is defined. (*Id.*) These profiles are shown as lines 40 and 42 in the ‘813 patent at Figure 4, reproduced on the next page and annotated for discussion purposes:

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The patentees have defined in the specification what they mean by "rendering uniform the radial absorbed dose profile of the emissions." *Phillips*, 415 F.3d at 1316 (claims must be read in light of the specification). In Figure 4, line 40 is a plot of the absorbed dose as a function of radial distance that would be obtained if there were no structure defining an inner volume, *i.e.*, if the entire spherical volume of the tumor were completely filled with radioactive fluid. (Col. 3:20-24.) Plot 42, by contrast, shows the absorbed dose as a function of radial distance when the radioactive fluid is contained within an inner volume (defined by a polymeric film wall) and is surrounded by a radiation absorbing material contained in the outer volume. (Col. 3:24-28.) According to the specification, "[c]omparing plots 40 and 42, by providing the concentric arrangement depicted, the absorbed dose profile in the space between the 2cm site and the wall of the outer balloon is maintained *much more uniform*, thus preventing over-treatment of body tissue at or close to the outer wall 36 of the instrument." (Col. 3:28-33 (emphasis added).) As Dr. Verhey explains, plot 42 in Figure 4 shows a smaller ratio of the absorbed dose at the wall of the tumor cavity to the dose at the 2cm depth of interest than plot 40. Thus, as the specification defines the term, "rendering uniform the radial

1 absorbed dose profile of the emissions” means modifying the ratio of the absorbed dose at a depth of
 2 interest in the target tissue to the dose at the surface of the tissue, as exemplified by the difference
 3 between the slopes of plots 40 and 42.

4 Xoft’s construction of this function is unreasonable because it excludes the preferred
 5 embodiments shown in the specification. “A claim construction that excludes a preferred embodiment
 6 . . . is ‘rarely, if ever, correct.’” *Pfizer, Inc. v. Teva Pharm. USA, Inc.*, 429 F.3d 1364, 1374 (Fed. Cir.
 7 2005) (quoting *SanDisk Corp. v. Memorex Prods., Inc.*, 415 F.3d 1278, 1285 (Fed. Cir. 2005));
 8 *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996) (same). In the diagram in
 9 Figure 4, the radial absorbed dose profile plot 42 does not show the same dose at every point along the
 10 radius, as Xoft would require. Rather, the ratio of the dose at the cavity wall to the dose at the depth of
 11 interest is less than that for the configuration in plot 40, consistent with Cytac’s construction.

12 The corresponding structure disclosed in the specification for performing this function is a
 13 radiation absorbing or attenuating material, e.g., air, x-ray contrast fluid, contrast media used in
 14 angiography, water, a gas, or barium sulfite. *Kahn*, 135 F.3d at 1476 (holding that structure described
 15 in the specification is corresponding structure if the specification “clearly links or associates that
 16 structure to the function recited in the claim.”). Xoft appears to agree, suggesting that the “substance
 17 within the outer chamber” corresponds to the function for making the radial absorbed dose profile
 18 more uniform.

19 **G. “The Radioactive Material” (Claim 8)**

Cytac’s Proposed Construction	Xoft’s Proposed Construction
The material of claim 1 containing a radionuclide.	Indefinite because no antecedent.

24 Again, Xoft offers no construction of this term, arguing only that it is indefinite. Xoft’s
 25 argument fails. Claim 8 depends from claim 1, and it is obvious that the “the radioactive material” in
 26 claim 8 clearly refers back to “a material containing a radionuclide” described in claim 1, given that
 27 the “radionuclide” is the only radioactive material mentioned in claim 1. Anyone skilled in the art
 28

1 would know that the “radioactive material” in claim 8 refers to the “material containing a radionuclide”
2 in claim 1. Claim 8 is therefore not indefinite.

H. “A Plurality Of Radioactive Solid Particles Placed At Pre-determined Locations Within The Inner Spatial Volume To Provide A Desired Composite Radiation Profile” (Claim 12)

Cytec's Proposed Construction	Xoft's Proposed Construction
A plurality of radioactive solid particles placed at pre-determined locations within the inner spatial volume to provide a desired dose profile that is the sum of the radiation profiles of the plurality of particles.	Static array of solid radioactive particles each placed in a single location and mounted on distal ends of separate wires. "Desired composite radiation profile" is indefinite.

Xoft's proposed construction of this term improperly imports limitations from the specification that are merely examples of the preferred embodiment. The ordinary meaning of this claim term, which Cytac proposes as the proper construction here, follows the language of the claim: "A plurality of radioactive solid particles placed at pre-determined locations within the inner spatial volume to provide a desired dose profile that is the sum of the radiation profiles of the plurality of particles." (See AHC at 286 (defining composite as "made up of distinct components; compound").)

II. TERMS IN THE ‘204 PATENT

The ‘204 patent, which is a continuation-in-part of the ‘813 patent, describes an apparatus for brachytherapy and a method of using it for interstitial delivery of radiation to diseased cells within the interstices of the tissue surrounding the cavity created by the surgical removal of proliferative tissue.

The apparatus includes a catheter body member having a proximal end and a distal end, an inner spatial volume proximate to the distal end of the catheter body member, an outer spatial volume defined by an expandable surface element proximate to the distal end of the body member, and surrounding and concentric with the inner spatial volume. In a preferred embodiment, a radiation source is disposed within the inner spatial volume.

The ‘204 patent describes a number of embodiments that can be used in the apparatus for delivering a therapeutic dose of radiation, including, without limitation, radioactive microspheres (FIG. 4), concentric non-spherical chambers (FIG. 5), a single solid radiation emitting material surrounded by an expandable cage defining the shape of the tumor cavity (FIG. 6), a radioactive fluid filling the

1 outer chamber (FIG. 7a), a radioactive fluid filling the inner chamber and the outer chamber filled with
 2 air or other radiation absorbing substance (FIG. 7b), and a single solid source surrounded by an outer
 3 chamber filled with a radiation absorbing substance (FIG. 7c). Figure 7d shows examples of radiation
 4 profiles which might be obtained by the embodiments shown in Fig. 7a-7c where the depth of interest
 5 is shown as 2cm from the surface of the outer volume. As can be seen, different embodiments can be
 6 used to vary the ratio of the dose at the prescribed depth to the dose at the wall of the cavity.

7 **A. “Interstitial” (All Asserted Claims)**

Cytyc's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Site in natural or surgically created cavity in body.

11
 12 Cytyc addresses the construction of this term in connection with its construction of the term
 13 “interstitial brachytherapy” below. Cytyc believes that a separate construction of this term divorced
 14 from the context of the surrounding claim language is neither required nor appropriate. *See Phillips*,
 15 415 F.3d at 1314.

16 **B. “Brachytherapy” (All Asserted Claims)**

Cytyc's Proposed Construction	Xoft's Proposed Construction
Radiation therapy delivered by a spatially confined radiation source at or near the site of the diseased tissue.	Radiation therapy delivered by a spatially confined radionuclide at or near a tumor or other proliferative tissue disease site.

17
 18 The parties mostly agree on the definition of “brachytherapy” with two exceptions. *First*, Xoft
 19 attempts to limit brachytherapy to the use of a “radionuclide” for irradiating tissue. But radiation can
 20 be provided from sources that are not radionuclides (but that can be equivalent to radionuclides), e.g.
 21 an X-ray tube. (*See Exhibit F to the Declaration of Henry C. Su (The Physics of Radiation Therapy) at*
 22 418 (“Brachytherapy is a method of treatment in which sealed radioactive sources are used to deliver
 23 radiation at a short distance by interstitial, intracavitary, or surface application.”).) There is no reason
 24 to limit brachytherapy to use of a radionuclide and Xoft’s construction should be rejected. *Second*,
 25 Xoft improperly attempts to limit brachytherapy to treatment of tumors or other proliferative tissue
 26
 27
 28

1 diseases. But there is no basis for such a limitation, as radiation can be applied to any diseased tissue
2 as a doctor believes appropriate.

C. "Interstitial Brachytherapy" (All Asserted Claims)

Cytec's Proposed Construction	Xoft's Proposed Construction
Brachytherapy applied directly to the interspaces of a body tissue, where the interspaces are not naturally occurring.	Radiation therapy delivered by a spatially confined radionuclide at or near a tumor site in a natural or surgically resected cavity in a body.

Xoft has, for almost all the other disputed terms in the ‘204 patent, improperly added limitations that are not supported by the terms’ plain meaning or the patent specification or prosecution history. With respect to “interstitial brachytherapy,” which the inventors specifically defined in the prosecution history as excluding certain types of therapies, Xoft now improperly redefines the term in a manner inconsistent with the inventors’ clear statements. Xoft may not blithely ignore the intrinsic evidence.

Specifically, Xoft's attempt to include "natural" body cavities in its definition of "interstitial brachytherapy" is directly contrary to the patent's prosecution history. During prosecution of the '204 patent, in traversing a rejection from the examiner, the inventors distinguished between brachytherapy applied to a natural body cavity and interstitial brachytherapy:

Turning to the cited prior art, the Ishiwara device comprises a thermotherapeutic apparatus having a catheter body member, an inner lumen surrounded by an outer lumen, and a radiation source contained within the inner lumen. As disclosed in col. 4, lines 19-23, Ishiwara's apparatus is inserted into a body cavity. . . . Hence the apparatus does not provide *interstitial* radiation treatment, as Applicant's invention requires, but rather intercavital radiation treatment.

(Exhibit E to the Declaration of Henry C. Su (12/20/00 Amendment and Response (“Amendment”)) at 11 (emphasis in original; internal citations omitted).)

Similarly, with respect to another reference, the inventors distinguished intraluminal therapy from interstitial therapy:

Weinberger discloses in Figure 17 an intercavital radiotherapy device for insertion within a patient's lumen. . . . Like Ishiwara, Weinberger's apparatus does not provide *interstitial* radiation treatment, as Applicant's invention requires, but instead *intraluminal* radiation treatment. Whereas Applicant's device treats disease that is

1 embedded in tissue (e.g., breast cancer), Ishiwara and Weinberger treat disease in a
 2 luminal cavity. For this reason, in Ishiwara and Weinberger, the catheters and
 3 expandable balloons are very different than those of Applicant's invention.

4 (Amendment at 12 (emphasis in original; internal citations omitted).) In light of these clear statements,
 5 Cytac is surprised that Xoft would even attempt to propose a construction of "interstitial
 6 brachytherapy" that included natural body cavities or lumens.

7 In summary, the inventors have specifically excluded "intercavital" or "intraluminal" radiation
 8 therapy – *i.e.*, insertion of a brachytherapy apparatus within a natural body cavity or lumen – from the
 9 definition of "interstitial brachytherapy." Cytac's proposed construction comports with the plain
 10 meaning of the claim term, based on the inventors' disclaimer in the prosecution history.

10 D. **"Inner Spatial Volume" (All Asserted Claims)**

Cytac's Proposed Construction	Xoft's Proposed Construction
.A region of space surrounded by an outer spatial volume that is defined by an expandable surface element.	Inner balloon in two-balloon device or spherical solid radionuclide in one-balloon device.

11 Xoft's attempt to limit the "inner spatial volume" to a "balloon" or a "spherical solid
 12 radionuclide" should be rejected. A "balloon" is not even one of the embodiments of the "inner spatial
 13 volume" described in the specification. Rather, as in the '813 patent, the specification of the '204
 14 patent describes, as an exemplary embodiment, that "the inner spatial volume 30 . . . *may* be defined
 15 by a generally spherical polymeric film wall 32." (Col. 3:58-59.) In any event, it is improper to limit
 16 the claim language to the embodiments in the specification, as Xoft proposes. *Phillips*, 415 F.3d at
 17 1323 (one must "avoid the danger of reading limitations from the specification into the claim.").

18 More fundamentally, Xoft continues to confuse the structure that defines an inner spatial
 19 volume with the volume itself. The specification provides that the inner spatial volume 30 "may be
 20 *defined by* a generally spherical polymeric film." The film defines the boundary of the volume but the
 21 volume is the region of space within that boundary. Thus, according to the specification, the inner
 22 spatial volume is simply a region of space surrounded by an outer spatial volume. (*See* col. 2:39-45
 23 ("The apparatus includes . . . an inner spatial volume disposed proximate to the distal end of the
 24 catheter body member, [and] an outer spatial volume defined by an expandable surface element

1 disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial
 2 volume”.)

3 Cytac’s proposed construction fully captures the plain meaning of “inner spatial volume,”
 4 which the Federal Circuit notes is of “primary importance” in claim construction. *Phillips*, 415 F.3d
 5 1312. A “spatial volume” is a commonly understood English term, meaning “a region of space.”
 6 (AHC at 1513 (defining “volume” as “the amount of space occupied by a three-dimensional object or
 7 region of space, expressed in cubic units”)). The word “inner” means that that region of space is
 8 located within something else, and the specification provides that that “something else” is another
 9 (outer) “spatial volume.” (Col. 1:52-55.) Thus, “inner spatial volume” should be construed to mean “a
 10 region of space surrounded by an outer spatial volume that is defined by a closed inflatable chamber.”

11 **E. “Outer Spatial Volume” (All Asserted Claims)**

Cytac’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Balloon or cage.
Alternatively: a region of space defined by an expandable surface element and surrounding an inner spatial volume.	

17 Cytac believes that no construction of this term is required or appropriate. The term has its
 18 ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic
 19 evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning
 20 to the term. Thus, “outer spatial volume” should be construed to mean “outer spatial volume.”

21 Xoft’s proposed construction of the term, like its proposed construction of “inner spatial
 22 volume,” confuses the outer spatial volume with the “expandable surface element” that defines its
 23 boundary. The “outer spatial volume” is a region of space that is *defined* by an “expandable surface
 24 element” but it is not the “expandable surface element” itself. (*See* col. 3:61-65.) If the Court is
 25 inclined to construe “outer spatial volume,” then the term should be construed as “a region of space
 26 defined by an expandable surface element and surrounding an inner spatial volume.” This is consistent
 27 with the ordinary meaning of the claim term in view of the specification.

1 **F. “Expandable Surface Element” (All Asserted Claims)**

Cytyc's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate. Alternatively: a device that can be expanded or inflated, such as an expandable cage or an inflatable balloon.	Deflated balloon or collapsed cage.

7 Cytyc believes that no construction of this term is required or appropriate. The term has its
8 ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic
9 evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning
10 to the term. “Expandable surface element” should be construed to mean “expandable surface
11 element.”

12 Xoft’s attempt to limit the term to a “deflated balloon or a collapsed cage” is improper, and
13 there is no support for doing so in any of the intrinsic evidence. Something that is “expandable” is
14 capable of expansion (or inflation) and can be in any state of expansion (or inflation) from no
15 expansion to full expansion. Indeed, as Dr. Verhey explains, a person having ordinary skill in the art
16 would expect to have to expand the expandable surface element in order to practice the invention of
17 the ‘204 patent. (Verhey Rep. at 9:17-20, 10:16-18.) A construction that limits this element to a
18 “deflated” or “collapsed” state is unreasonable and erroneous.

19 **G. “Radiation Source” (All Asserted Claims)**

Cytyc's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Radionuclide

23 Cytyc believes that no construction of this term is required or appropriate. The term has its
24 ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic
25 evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning
26 to the term. A “radiation source” is simply that—a radiation source. Xoft’s attempt to limit a
27 “radiation source” to just radionuclides, a specific kind of source, is unsupportable.

1 **H. “Minimum Prescribed Dose” (Claims 2, 18, 24, 32, & 36)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
Minimum prescribed dose received within a target tissue for delivering therapeutic effects.	Minimum dose needed to treat cancer cells.

6 Xoft’s attempt to limit this term to the provision of a dose to treat cancer cells is improper and
 7 unsupported. The term has its ordinary and customary meaning to one skilled in the art without
 8 reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by the inventors to
 9 impart a novel or special meaning to the term. The meaning can be readily discerned from the context
 10 of the surrounding claim language – “a minimum prescribed absorbed dose for delivering therapeutic
 11 effects to a target tissue.” (See, e.g., col. 8:31-33.) *See also Phillips*, 415 F.3d at 1314 (“Quite apart
 12 from the written description and the prosecution history, the claims themselves provide substantial
 13 guidance as to the meaning of particular claim terms. . . . To begin with, the context in which a term is
 14 used in the asserted claim can be highly instructive.”)

15 **I. “Delivering A Prescribed Absorbed Dose” (Claim 34)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Indefinite – the patent contains no information on how to obtain a prescribed dose, much less a prescribed dose using an expandable surface element.

21 Cytyc believes that no construction of this term is required or appropriate. The term has its
 22 ordinary and customary meaning to one skilled in the art without reference to intrinsic or extrinsic
 23 evidence, and there is no evidence of any intent by the inventors to impart a novel or special meaning
 24 to the term. Contrary to Xoft’s assertion, the phrase is not indefinite because a “prescribed absorbed
 25 dose” refers to the fact that the amount of the dose to be delivered to a target tissue is within the
 26 discretion (i.e., prescription) of a person with ordinary skill in the art to determine. For example, a
 27 radiation oncologist determines, using treatment planning software or some other reference or tool, the
 28 proper dosage for each patient, depending on a number of physiological factors. The patient-specific

1 amount of radiation is a “prescribed dose.” As to how the dose is delivered, Dr. Verhey explains that
 2 “once the inflatable expandable surface element is in contact with the surface of the surgical cavity, the
 3 dose at the prescription depth can be delivered once the radiation source is introduced into the
 4 catheter.” (Verhey Rep. at 9:26-28 (citing col. 5:66 – 6:28).) Delivering a prescribed absorbed dose is
 5 not indefinite and the term means exactly what it says—delivering a prescribed absorbed dose.

6 **J. “The Inner And Outer Spatial Volumes Are Configured To Provide A**
 7 **Minimum Prescribed Absorbed Dose” (Claim 2 & 36) And “Configuring**
 8 **The Inner And Outer Spatial Volumes To Provide A Minimum Prescribed**
 9 **Absorbed Dose” (Claims 24 & 32)**

Cytec's Proposed Construction	Xoft's Proposed Construction
<p>10 The inner and outer spatial volumes are 11 configured to provide a minimum prescribed 12 absorbed dose for delivering therapeutic effects 13 to a target tissue; 14 and 15 Configuring the inner and outer spatial 16 volumes to provide a minimum prescribed 17 absorbed dose for delivering therapeutic effects 18 to a target tissue.</p>	<p>Indefinite – configured volumes are expanded 19 volumes, but no cause and effect relationship 20 between configuring of inner and outer 21 volumes and providing dose of any prescribed 22 amount.</p>

19 Contrary to Xoft’s contention, this term is not indefinite. The ‘204 patent discloses in detail the
 20 various ways in which a person of ordinary skill in the art can achieve a configuration of the inner and
 21 outer spatial volumes that will deliver a minimum prescribed dose to a target tissue of interest. (See,
 22 e.g., col. 5:22-41; col. 6:16 – col. 7:28.) As Dr. Verhey explains:

23 [W]here the radioactive material is disposed in the inner spatial volume, the rate at
 24 which the dose falls off between the surface of the surgical cavity and the depth at
 25 which the minimum dose is to be prescribed, can be controlled by modifying the
 26 quantity and type of radiation absorbing material contained within the outer spatial
 27 volume. The safe delivery of the minimum prescribed dose at the depth of interest
 28 requires that the tissue intervening between the surface of the cavity and the depth of
 29 interest receive a dose which is equal to or greater than the prescribed dose but less than
 30 that which would necrose (i.e., lethally damage) healthy tissue.”

(Verhey Rep. at 8:25 – 9:3.) Because one skilled in the art knows how to configure the spatial
 21 volumes to provide the minimum prescribed absorbed dose, the term is not indefinite.

1 **K. “A Minimum Distance Outward From The Outer Spatial Volume**
 2 **Expandable Surface” (Claims 2, 24, 32, & 36)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Indefinite because it is some unknown distance from deflated balloon or collapsed cage. Patent contains no information regarding determination of minimum distance.

8 Cytyc believes that no construction of this term is required or appropriate and that the term is
 9 definite. The term has its ordinary and customary meaning and is understood by one of ordinary skill
 10 in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by
 11 the inventors to impart a novel or special meaning to the term.

12 The meaning of “a minimum distance outward from the outer spatial volume expandable
 13 surface” is not indefinite and can be readily discerned from the context of the surrounding claim
 14 language – “the target tissue being defined between the outer spatial volume expandable surface and a
 15 minimum distance outward from the outer spatial volume expandable surface.” The disputed phrase
 16 refers to the minimum distance outward from the expandable surface element that defines the outer
 17 spatial volume. This minimum distance defines the thickness of a layer of target tissue which, in the
 18 determination of a person of ordinary skill in the art, includes the region in which diseased cells might
 19 reside. (Verhey Rep. at 9:6-9.)

20 **L. “Controlled Dose” (Claim 2, 24, 32, & 36)**

Cytyc’s Proposed Construction	Xoft’s Proposed Construction
No construction required or appropriate.	Indefinite because configuration, i.e., expansion, of inner and outer volumes does not control dose.

25 Cytyc addresses the construction of this term in connection with its construction of the phrase
 26 “providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent
 27 necrosis in healthy tissue proximate to the expandable surface” below. Cytyc believes that a separate
 28

1 construction of this term divorced from the context of the surrounding claim language is neither
 2 required nor appropriate.

3 **M. “To Reduce Or Prevent Necrosis In Healthy Tissue Proximate To The**
 Expandable Surface” (Claims 2, 24, 32, & 36)

Cytyc's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Indefinite – patent does not describe providing a dose through expandable surface – improper functional limitation in apparatus claim.

9 Cytyc addresses the construction of this term in connection with its construction of the phrase
 10 “providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent
 11 necrosis in healthy tissue proximate to the expandable surface” below. Cytyc believes that a separate
 12 construction of this term divorced from the context of the surrounding claim language is neither
 13 required nor appropriate.

14 **N. “Providing A Controlled Dose At The Outer Spatial Volume Expandable**
 Surface To Reduce Or Prevent Necrosis In Healthy Tissue” (Claims 2, 24,
 32 & 36)

Cytyc's Proposed Construction	Xoft's Proposed Construction
Controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface	Indefinite because radiation dose is not provided when outer volume surface is “expandable”, i.e., is a deflated balloon or a collapsed cage. Also indefinite because patent contains no information on how to provide dose that will reduce or prevent necrosis in healthy tissue. In context, the word “necrosis” and the term “necrosis in healthy tissue” are indefinite.

23 Xoft does not offer a construction of this disputed term; it only argues that the term is
 24 indefinite. But the term is well understood by those of skill in the art. Dr. Verhey explains that by
 25 adjusting the distance between the radiation source and the surface of the outer spatial volume, or by
 26 adjusting the type of radiation absorbing material in the outer spatial volume, the ratio of the dose at
 27 the surface of the outer spatial volume to the prescribed dose at the depth of prescription can be
 28

1 controlled. (Verhey Rep. at 9:12-15.) The dose must not be so high that it causes necrosis to occur in
 2 healthy tissue that is in contact with the expandable surface; persons of skill in the art will know how
 3 high such a dose may be before a significant percentage of healthy cells necrose. (*Id.*)

4 **O. “Adapting The Expandable Surface To Contact Tissue Surrounding The**
 Resection Cavity To Conform The Tissue” (Claim 34)

Cytyc's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Indefinite because expandable surface, i.e., deflated balloon or collapsed cage, neither contacts nor conforms the tissue surrounding the resection cavity. The patent contains no information on how this could be done.

11 Cytyc believes that no construction of this term is required or appropriate and that the term is
 12 definite. The term has its ordinary and customary meaning and is understood by one of ordinary skill
 13 in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by
 14 the inventors to impart a novel or special meaning to the term. The term “adapting the expandable
 15 surface to contact tissue surrounding the resection cavity to conform the tissue to the desired shape of
 16 the expandable surface element” means adapting the expandable surface so that it comes into contact
 17 with the tissue forming the wall of the resection cavity and conforms that tissue to its shape. This
 18 comports with the ordinary meaning of the claim term.

19 Xoft’s indefiniteness assertion is premised on its flawed construction of “expandable surface,”
 20 which requires that the surface be in a deflated or collapsed state. The fact that claim 34, however,
 21 requires the expandable surface to contact the tissue surrounding the resection cavity establishes that
 22 Xoft’s construction of “expandable surface” is erroneous. Under a proper construction, the expandable
 23 surface can be inflated or expanded to some degree so that it contacts the tissue and conforms the
 24 tissue to its shape. Dr. Verhey explains: “the volume of the expandable surface can be adjusted by
 25 inflation until the surface of the expandable volume is in contact with the surface of the resection
 26 cavity at all points. In this state, the shape of the resection cavity conforms to the shape of the
 27 expandable surface.” (Verhey Rep. at 9:18-20 (citing col. 5:47-61).)

28 //

1 **P. “Desired Shape Of The Expandable Surface Element” (Claims 4, 26, & 34)**

Cytyc's Proposed Construction	Xoft's Proposed Construction
The desired shape of the expandable surface element.	Indefinite. Patent contains no information regarding the desired shape of an expandable surface element, i.e., a deflated balloon or collapsed cage.

7 Cytyc believes that no construction of this term is required or appropriate and that the term is
 8 definite. The term has its ordinary and customary meaning and is understood by one of ordinary skill
 9 in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by
 10 the inventors to impart a novel or special meaning to the term.

11 This term is not indefinite, as Xoft wrongly contends. The desired shape of the balloon is
 12 within the discretion of those skilled in the art. According to Dr. Verhey, “the desired shape of the
 13 expandable surface element is that shape which provides the predetermined constant spacing between
 14 the inner spatial volume and the conformed surface of the resection cavity.” (Verhey Rep. at 9:22-24
 15 (citing col. 5:47-61).) Examples of desired shapes described in the specification include a spherical
 16 balloon (FIG. 1) and a cylindrical balloon (FIG. 5), but the invention is not limited to any particular
 17 shape. (Col. 5:13-16.)

18 **Q. “Predetermined Spacing” (Claims 3 & 25)**

Cytyc's Proposed Construction	Xoft's Proposed Construction
No construction required or appropriate.	Indefinite because no information in patent re how to determine “predetermined spacing.” Also indefinite because spacing is between inner spatial volume and expandable surface element, i.e., deflated balloon or collapsed cage.

24 Cytyc addresses the construction of this term in connection with its construction of the phrase
 25 “a predetermined spacing is provided between said inner spatial volume and the expandable surface
 26 element” below. Cytyc believes that a separate construction of this term divorced from the context of
 27 the surrounding claim language is neither required nor appropriate.
 28

1 **R. “A Predetermined Spacing Is Provided Between Said Inner Spatial Volume**
 2 **And The Expandable Surface Element”/ “A Predetermined Spacing**
 3 **Between Said Inner Spatial Volume And The Expandable Surface**
 4 **Element” (Claims 3 & 25)**

Cytyc's Proposed Construction	Xoft's Proposed Construction
The distance between the inner spatial volume and the expandable surface element is determined in advance.	A predetermined spacing between inner spatial volume and deflated balloon or collapsed cage is indefinite.

8 Cytyc believes that no construction of this term is required or appropriate and that the term is
 9 definite. The term has its ordinary and customary meaning and is understood by one of ordinary skill
 10 in the art without reference to intrinsic or extrinsic evidence, and there is no evidence of any intent by
 11 the inventors to impart a novel or special meaning to the term.

12 Contrary to Xoft’s assertion, the term is not indefinite and has an ordinary and customary
 13 meaning to one skilled in the art. Dr. Verhey readily understood the term to mean that the spacing
 14 between the inner and outer volumes can be set to a predetermined value by modifying the level of
 15 inflation or expansion of one or both volumes. Although Xoft incorrectly suggests that the patent must
 16 describe that amount of spacing, a patent does not need to describe what one skilled in the art already
 17 knows and can practice. *See S3 Inc. v. nVidia Corp.*, 259 F.3d 1364, 1371 (Fed. Cir. 2001). One
 18 skilled in the art knows how to determine an appropriate “predetermined spacing.”

19 Moreover, to the extent Xoft contends that there can be no spacing between the inner volume
 20 and a deflated balloon or collapsed cage, that argument also fails. Such an argument is premised on
 21 the erroneous proposal that “expandable surface” be limited to a deflated or collapsed surface.
 22 Because that construction is inconsistent with the patent and must be rejected for the reasons set forth
 23 above (*see supra* at II.F), Xoft’s indefiniteness argument must also fail.

24 //

25 //

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1 **S. “Intraoperatively” (Claims 19 & 34)**

Cytec's Proposed Construction	Xoft's Proposed Construction
Intraoperatively	After surgical removal of tumor but prior to closing the surgical site.
Alternatively: during the surgical operation to remove proliferative tissue	

7 The parties appear to agree for the most part as to the meaning of “intraoperatively,” and Cytec
 8 could agree to Xoft’s proposed construction if only the construction does not include “closing the
 9 surgical site,” which is superfluous. “Intraoperatively” simply means during the surgical operation to
 10 remove the proliferative tissue. Whether the site is subsequently closed (*e.g.*, with sutures) is
 11 irrelevant.

12 **T. “Solid Radiation Source” (Claim 16)**

Cytec's Proposed Construction	Xoft's Proposed Construction
A radiation source that has a fixed shape and volume, and is not deformable.	Solid radionuclide

16 Xoft again improperly attempts to limit a radiation source to a radionuclide. There are other
 17 sources of radiation besides radionuclides, and there is no basis in the intrinsic evidence for limiting
 18 the plain meaning of “radiation source” to a radionuclide. Moreover, Xoft neglects to define “solid,”
 19 which refers to the fact that the radiation source that has a fixed shape and volume and is not
 20 deformable. (*See* AHC at 1295 (“of definite shape and volume; not liquid or gaseous”); Verhey Rep.
 21 at 11:8-9.)

22 **U. “The Prescribed Absorbed Dose Is Delivered To The Target Tissue In
 23 Substantially Three Dimensions” (Claim 18)**

Cytec's Proposed Construction	Xoft's Proposed Construction
The prescribed absorbed dose is delivered to the target tissue such that all points at a given outward distance from the tissue wall will receive the same dose.	Prescribed absorbed dose is indefinite and substantially three dimensional is indefinite.

Contrary to Xoft's assertion, there is nothing indefinite about this limitation because one of ordinary skill in the art would understand what a prescribed absorbed dose is and how that dose can be delivered substantially in three dimensions. Dr. Verhey explains that this limitation relates to the fact that, once the outer chamber is expanded, the tissue in contact with the chamber conforms to the shape of the chamber, thereby assuring that all points within the tissue that are at a fixed distance from the wall of the surgical cavity will receive the identical dose. (Verhey Rep. at 11:12-15.) In this manner, the prescribed dose is delivered to the target tissue at the depth of interest substantially in all three dimensions, as opposed to being delivered in only two dimensions (to all points on a plane) or one dimension (to all points along a line). The limitation is clear, not indefinite, and should be given its ordinary meaning.

CONCLUSION

12 For the reasons stated above, this Court should adopt Cytec's proposed constructions of the
13 disputed terms of the '813 and '204 patents, and reject Xoft's proposed constructions and
14 indefiniteness arguments.

Respectfully submitted,

DATED: November 9, 2006

HOWREY LLP

By:/s/ Henry C. Su
Henry C. Su

Attorneys for Defendants CYTYC CORPORATION and CYTYC SURGICAL PRODUCTS II, INC.

CERTIFICATE OF SERVICE

As required by Civil Local Rule 5-6(a)(2), the undersigned hereby certifies that on November 9, 2006, a true and correct copy of:

**DEFENDANT AND COUNTERCLAIMANT CYTYC CORPORATION'S
OPENING CLAIM CONSTRUCTION BRIEF (PAT. L.R. 4-5(a))**

was served on the following counsel of record for Xoft, Inc. electronically through this Court's Electronic Case Filing System, in accordance with Civil Local Rule 5-5(b):

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EXHIBIT F

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IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

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XOFT, INC.,

No. C-05-05312 RMW

Plaintiff,

CLAIM CONSTRUCTION ORDER

v.

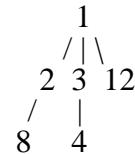
CYTYC CORPORATION; and PROXIMA
THERAPEUTICS, INC.,

[Re Docket Nos. 48, 50, 53]

Defendants.

Xoft, Inc. sued Cytac Corporation and one of its subsidiaries, Cytac Surgical Products II, Inc., (collectively "Cytac") for a declaratory judgment of non-infringement and invalidity of U.S. Patent Nos. 5,913,813 and 6,413,204. Cytac responded by filing counterclaims for infringement of the same patents and currently asserts that Xoft infringes six claims of the '813 patent¹ and twenty

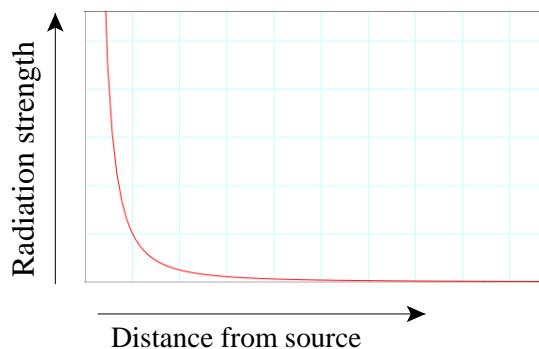
¹ Cytac asserts claims 1, 2, 3, 4, 8, and 12. Claim 1 is an apparatus claim and the only independent claim of the '813 patent. Claims 2, 3, and 12 depend directly from claim 1. Claim 4 depends from claim 3, and claim 8 depends from claim 2. The following is a graphic representation of the relationship of the asserted claims:



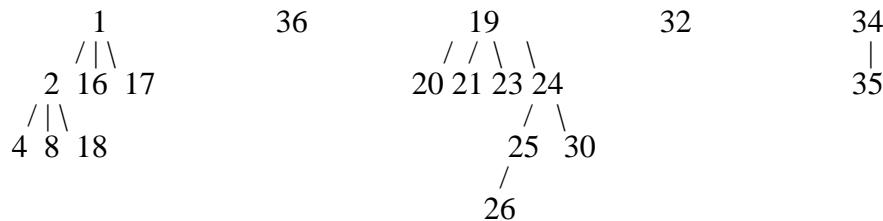
1 claims of the '204 patent². The application for the '204 patent was filed as a continuation-in-part of
 2 the '813 patent; the former purports to incorporate by reference the latter. '204 patent, col. 1, ll. 10-
 3 11. The parties seek construction of eight terms or phrases from the '813 patent and twenty-one
 4 terms or phrases from the '204 patent.

5 I. BACKGROUND

6 The patents-in-suit are directed to methods and apparatus for treatment of proliferative tissue
 7 diseases. The prior art discloses that a radiation source can be implanted at a tumor site to irradiate
 8 any remaining diseased tissue; this process is known as interstitial brachytherapy. The parties agree
 9 that for the purposes of this suit, the strength of radiation may be assumed to decrease with the
 10 square of the distance from the radiation source. The graph of the equation $y = 1/x^2$ thus can be
 11 used as an approximation of the relationship between the radiation strength and distance. The graph,
 12 shown below, illustrates that the radiation strength close to the radiation source is disproportionately
 13 higher than that at a relatively small distance away from the radiation source.

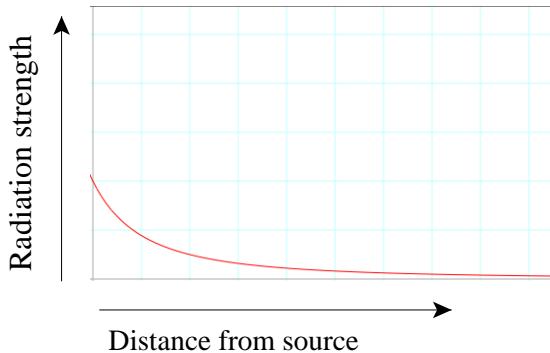


21 ² Cytc asserts claims 1, 2, 3, 4, 8, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 30, 32, 34, 35, and 36 of the
 22 '204 patent. Claims 1 and 36 are the only independent apparatus claims. From claim 1 depend
 23 claims 2, 16, and 17. From claim 2 depend claims 4, 8, and 18. Claims 19, 32, and 34 are
 24 independent method claims. Claims 20, 21, 23, and 24 all depend from claim 19. Claim 25 depends
 25 from claim 24, and claim 26 depends from claim 25. Claim 30 also depends from claim 24. Claim
 35 depends from claim 34. The following is a graphic representation of the relationship of the
 asserted claims:



1 This shows one of the problems encountered in radiation therapy, namely, that tissue close to
 2 the radiation source may get more radiation than a physician would prefer. When using interstitial
 3 therapy, a physician may wish to give all tissue within a certain distance—say, for example, 3
 4 centimeters—from the tumor site a certain dose of radiation. However, tissue closer to the tumor
 5 site—say, 1 centimeter—will receive a much higher dose of radiation because of the inverse-square
 6 relationship. This means that healthy tissue near the tumor site may be killed by the radiation, which
 7 is an undesirable result.

8 Following the teachings of the patents-in-suit, the very high levels of radiation near the
 9 source can be avoided by simple mechanical means. Surrounding the radiation source on all sides
 10 with empty space (or some material other than living tissue) prevents the highest levels of radiation
 11 from affecting living tissue, giving the tissue a radiation dose profile that looks something like this:



II. ANALYSIS

A. Terms of the '813 patent

"Inner spatial volume"

Cytyc's proposed construction	Xoft's proposed construction
A region of space surrounded by an outer spatial volume that is defined by a closed inflatable chamber	Inner balloon in two-balloon device or spherical solid radionuclide in one-balloon device

25 The summary of the invention provides that

26 it is possible to deliver a desired radiation dose at a predetermined radial distance
 27 from a source of radioactivity by providing a first spacial^[3] volume at the distal end
 of a catheter and a second spacial volume defined by a surrounding of the first spatial

28 ³ Presumably all occurrences of "spacial" in the '813 patent should be read as "spatial."

volume by a polymeric film wall where the distance from the spatial volume^[4] and the wall is maintained substantially constant over their entire surfaces. One of the inner and outer volumes is filled with either a fluid or a solid containing a radionuclide(s) while the other of the two volumes is made to contain either a low radiation absorbing material, e.g., air or even a more absorptive material, such as an x-ray contrast fluid. Where the radioactive material comprises the core, the surrounding radiation absorbing material serves to control the radial profile of the radioactive emissions from the particular one of the inner and outer volumes containing the radionuclide(s) so as to provide a more radially uniform radiation dosage in a predetermined volume surrounding the outer chamber. Where the core contains the absorbent material, the radial depth of penetration of the radiation can be tailored by controlling the core size.

'813 patent, col. 1, l. 50-col. 2, l. 3. The first two claims of the '813 patent read:

1. Apparatus for delivering radioactive emissions to a body location with a uniform radiation profile, comprising:
 - (a) a catheter body member having a proximal end and distal end;
 - (b) an inner spatial volume disposed proximate the distal end of the catheter body member;
 - (c) an outer, closed, inflatable, chamber defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall;
 - (d) a material containing a radionuclide(s) disposed in one of the inner spatial volume and outer chamber; and
 - (e) means disposed in the other of the inner spatial volume and outer chamber for rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber containing the radionuclides.
2. The apparatus as in claim 1 wherein said inner spatial volume is an inner closed, chamber defined by a further radiation transparent wall.

'813 patent, col. 4, ll. 32-54. Since all claims of this patent other than claim 1 depend from claim 1, construction of "inner spatial volume" is critical.

In most embodiments of the invention disclosed in the patent specification, the inner spatial volume is a region of space surrounded by an outer spatial volume that is defined by a closed inflatable chamber. *See* '813 patent, col. 2, ll. 44-63; col. 3, ll. 9-16, 42-48; col. 4, ll. 16-20; figs. 1,

⁴ Presumably this "spatial volume" should be taken to be the first spatial volume, which would mean that the polymeric film wall forms the outer boundary of the second spatial volume and that the second spatial volume is of a uniform thickness on all sides of the first spatial volume. Such a reading would comport with claim 1(c).

1 3-5. However, the patentee drafted the claims in such a way as to make clear that the inner spatial
 2 volume was not necessarily so limited:

3 Those skilled in the art will appreciate that instead of having the inner spatial volume
 4 **30** defined by a generally spherical polymeric film wall as at **32**, the catheter body
 5 member **12** may have a solid spherical radiation emitting material in which event that
 6 solid sphere would be surrounded with the outer spherical wall **36** with the spatial
 7 volume therebetween occupied by a radioactive ray absorbent material, such as air,
 8 water or a contrast material.

9 '813 patent, col. 2, ll. 55-63.

10 Although somewhat awkwardly worded, the language of the patent allows for the inner
 11 volume to be defined by something other than a region enclosed by a polymeric wall. As Cytac
 12 points out, Xoft's construction conflates the boundary of the volume with the volume itself. Cytac's
 13 proposed construction, however, is a paraphrasing of the language of claim 1 that only clarifies a
 14 little the language of the patent. Furthermore, Cytac's proposed construction would exclude an inner
 15 volume defined by a solid sphere, and thus cannot be correct.

16 Xoft objects that an abstract concept like a region of space cannot be part of an apparatus.
 17 Xoft is correct. However, the language of the patent does not imply that the inner volume is ever
 18 defined by something other than a physical object. In all embodiments of the invention disclosed in
 19 the '813 patent, the boundary of the inner volume is either a polymeric film wall or the edge of a
 20 solid sphere. Furthermore, it would seem difficult to fill one volume with radioactive liquid and the
 21 other with another fluid if the two volumes were not separated by some structure (which would
 22 necessarily be the outer boundary of the inner spatial volume.) *See* '813 patent, col. 1, ll. 57-62. The
 23 patent is even entitled "Double-Wall Balloon Catheter for Treatment of Proliferative Tissue." Xoft's
 24 expert, Dr. Lovoi, acknowledged that an "inner spatial volume" is a volume that is inside another
 25 volume. Lovoi Dep. at 101:25-102:7. The court defines "inner spatial volume" as "a region of
 26 space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined
 27 by the edge of a solid radionuclide sphere."

<i>Claim Language</i>	<i>Court's Construction</i>
"inner spatial volume"	a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere

"Outer, closed, inflatable chamber"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	Inflatable balloon, i.e., deflated balloon

Part (c) of claim 1 explains that the "outer, closed, inflatable chamber" is "defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall." '813 patent, col. 4, ll. 40-45. The preferred embodiment recites a similar structure: "Surrounding the spatial volume **30** is an outer chamber **34** defined by an outer polymeric film wall **36** that is appropriately spaced from the wall **32** of the inner chamber **30** when the two chambers are inflated or otherwise filled and supported." '813 patent, col. 2, ll. 37-41. There is no support in the patent for Xoft's argument that "outer, closed, inflatable chamber" should be limited to only a balloon in a deflated state. The court will therefore adopt Cytyc's proposal and not otherwise define this term.

<i>Claim Language</i>	<i>Court's Construction</i>
"outer, closed, inflatable chamber"	outer, closed, inflatable chamber

"Predetermined constant spacing"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

"Predetermined constant spacing between said inner spatial volume and radiation transparent wall"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
The spacing between the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, can be made constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical	(indefinite)

Xoft argues that the '813 patent is indefinite because it does not disclose how one "predetermines" the amount of spacing. Xoft points out that the spacing between the edges of the inner and outer volumes may change as parts of the apparatus are inflated or deflated, so the spacing is not constant. Cytyc's expert explained that "predetermined constant spacing" means that "the

1 spacing between the inner spatial volume and the wall of the outer inflatable chamber can be made
 2 constant in all directions if the outer chamber is spherical, or constant along a radial direction if non-
 3 spherical, whenever the outer chamber is inflated." Su Decl. (dkt. # 49), Ex. D (Verhey Decl.) at 7
 4 (citations omitted). Cytac also argues that "[o]ne skilled in the art knows how to determine an
 5 appropriate 'predetermined constant spacing' and Xoft provides no evidence, testimony, or case law
 6 to the contrary. Xoft cannot possibly show that the term is indefinite by clear and convincing
 7 evidence." Reply Br. (dkt. # 53) at 15.

8 Because 35 U.S.C. § 282 gives a patent "a statutory presumption of validity," a challenger
 9 bears the burden of proving "by clear and convincing evidence" that a patent is invalid. *Monsanto*
 10 *Co. v. Scruggs*, 459 F.3d 1328, 1336-37 (Fed. Cir. 2006). "[P]atent documents need not include
 11 subject matter that is known in the field of the invention." *S3 Inc. v. NVIDIA Corp.*, 259 F.3d 1364,
 12 1371 (Fed. Cir. 2001). From the testimony of Dr. Verhey, it appears that one skilled in the art would
 13 know how to "predetermine" the amount of spacing.⁵ See Tr. at 56-61, 85-89. Xoft offered no
 14 evidence suggesting otherwise. As the burden of proof is Xoft's, its indefiniteness argument
 15 necessarily fails given the absence of supporting evidence. The court will therefore adopt Cytac's
 16 proposed construction of "predetermined constant spacing between said inner spatial volume and
 17 radiation transparent wall" modified only to make the definition easier to understand. A separate
 18 construction for "predetermined constant spacing" is not necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"predetermined constant spacing"	(no construction necessary)
"predetermined constant spacing between said inner spatial volume and radiation transparent wall"	spacing predetermined by one skilled in the art between the wall or edge of the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, which is constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical

27
 28 ⁵ Xoft argues that the size of the cavity determines the size of the apparatus when fully inflated, but this alone does not determine the spacing between the inner spatial volume and the wall of the outer chamber.

1 **"Rendering uniform"**

2 <i>Cytyc's proposed construction</i>	3 <i>Xoft's proposed construction</i>
(no construction required)	Making the same, i.e., causing to have the same value or characteristic at all points.

4 **"Means . . . for rendering uniform the radial absorbed dose profile of the emissions"**

5 <i>Cytyc's proposed construction</i>	6 <i>Xoft's proposed construction</i>
<p>Function: Modifying the ratio of the absorbed dose at a depth of interest in the target tissue to the absorbed dose at the surface of the tissue.</p> <p>Structure: A radiation absorbing or attenuating material, e.g., air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfate.</p>	<p>Function: Making the dose along a radius extending from the radionuclide outwardly from the outer chamber wall the same at every point on the radius.</p> <p>Structure: No such means disclosed in '813 patent, means for making more uniform disclosed as substance within outer chamber.</p>

11 Xoft's argument is that "uniform" must be taken literally, and the apparatus must produce
 12 radiation that does not decrease in strength with increasing distance from the source.⁶ The parties do
 13 not dispute that Xoft's construction would require a physical impossibility; the strength of radiation
 14 necessarily decreases with distance from its source. Xoft, however, seeks to interpret "uniform" in a
 15 vacuum. The meaning of a particular word in a claim must be interpreted in light of the rest of the
 16 patent. *Ekchian v. Home Depot, Inc.*, 104 F.3d 1299, 1303 (Fed. Cir. 1997).

17 While the patent could have been drafted with more clarity, it is readily apparent that the
 18 patentee did not contemplate absolute uniformity. Figure 4 of the patent (reproduced below) is a
 19 comparison between the distance versus radiation dose plots of two scenarios. Line 40 shows the
 20 radiation dose that would result if chamber 36 were filled with a radioactive fluid. '813 patent, col.
 21 3, ll. 20-24. Line 42 shows the radiation dose that would result if, following the teachings of the
 22 patent, the same radioactive fluid were contained only in chamber 32. '813 patent, col. 3, ll. 24-28.
 23 As explained in the patent, "Comparing the plots 40 and 42, by providing the concentric
 24 arrangement depicted, the absorbed dose profile in the space between the 2 cm site and the wall of
 25 the outer balloon is maintained much more uniform, thus preventing over-treatment of body tissue at
 26 27

28 ⁶ Xoft also stated that it would "submit a Motion for Summary Judgment on this issue prior to the conduct of the *Markman* hearing," Responsive Br. (dkt. # 50) at 14, but did not do so.

1 or close to the outer wall 36 of the
2 instrument." '813 patent, col. 3, ll.
3 28-33.

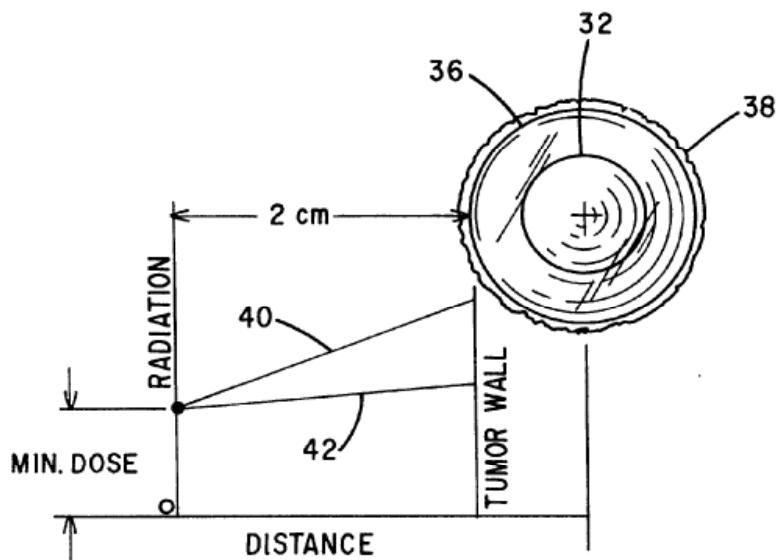
4 The patentee obviously did
5 not expect absolute uniformity of
6 radiation dosing. To interpret
7 "uniform" in the manner urged by
8 Xoft would go against the clear
9 intent of the patentee. In *Bausch &*

10 *Lomb, Inc. v. Barnes-*

11 *Hind/Hydrocurve, Inc.*, 796 F.2d

12 443 (Fed. Cir. 1986), the defendant made a similar argument regarding the patentee's use of the term
13 "smooth" with respect to the edges of contact lenses. The Federal Circuit looked to the intrinsic
14 evidence and found that "smooth" did not mean absolutely ridge free but rather that it meant
15 "smooth enough to serve the inventor's purposes, i.e., not to inflame or irritate the eyelid of the
16 wearer or be perceived by him at all when in place." *Id.* at 450. In this case, the inventor's purpose
17 was to deliver radiation more uniformly than had previously been done, "thus preventing over-
18 treatment of body tissue at or close to the outer wall . . . of the instrument." '813 patent, col. 3, ll.
19 28-32. The court will therefore define "rendering uniform" to mean to make the absorbed dose of
20 radiation more uniform in order to prevent over-treatment of body tissue at or close to the outer wall
21 of the instrument.

22 Since limitation language "means . . . for rendering uniform the radial absorbed dose profile
23 of the emissions" is in means-plus-function format, the function must be construed and the
24 corresponding structure or its equivalent identified in the specification. *BBA Nonwovens*
25 *Simpsonville, Inc. v. Superior Nonwovens*, L.C.C., 303 F.3d 1332, 1343 (Fed. Cir. 2002). As
26 discussed, Xoft's definition of the function requires absolute uniformity which is not possible and
27 which is not what the patent requires or the inventor intended. Cytc's proposed definition construes
28 the function as "modifying the ratio of the absorbed dose at a depth of interest in the target tissue to



1 the absorbed dose at the surface tissue." Although this appears to be a function of the invention,
 2 Cytac's definition is too broad because it encompasses absorbed doses at the surface tissue that are
 3 not substantially uniform to absorbed doses at the target tissue. In other words, Cytac's definition
 4 would not only encompass the radiation dose profile of line 42 above, but would also encompass the
 5 radiation dose profile of line 40. Furthermore, all radiation dose profiles between line 40 and line
 6 42 that result in over-treatment of the surface tissue would also be included under Cytac's definition.
 7 A more accurate construction of the function would require the absorbed dose at the target tissue and
 8 the absorbed dose at the surface tissue to be more uniform to prevent over-treatment of the surface
 9 tissue. Thus, the court defines the function of the "means . . . for rendering uniform the radial
 10 absorbed dose profile of the emissions" as making the absorbed dose of radiation more uniform to
 11 prevent over-treatment of body tissue at or close to the outer wall of the instrument.

12 Cytac also identifies a radiation-absorbing or -attenuating material as the corresponding
 13 structure. At the claim construction hearing, Xoft argued that the uniformity of the radiation dose
 14 curve is solely affected by distance from the radiation source; the parties agree that this is true. *See*
 15 Tr. at 60-61. Although the composition of the material is not critical to the function, the radiation-
 16 absorbing or -attenuating material provides the distance necessary for achieving the uniformity in
 17 radiation dose curve. Thus, the court construes the language consistently with Cytac's position.

<i>Claim Language</i>	<i>Court's Construction</i>
"rendering uniform"	to make the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument
"Means . . . for rendering uniform the radial absorbed dose profile of the emissions"	Function: Making the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument. Structure: A radiation absorbing or attenuating material, <i>e.g.</i> , air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfate or their equivalents.

"The radioactive material"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
The material of claim 1 containing a radionuclide.	(indefinite)

Claim 8 of the patent covers "[t]he apparatus as in claim 2 wherein the inner chamber contains the radioactive material." Claim 2 depends from claim 1. The parties dispute whether "a material containing a radionuclide(s)" suffices as an antecedent basis for "the radioactive material." It is readily apparent that the "radioactive material" in claim 8 refers back to "a material containing a radionuclide" described in claim 1, since "radionuclide" is the only radioactive material mentioned in claim 1. Anyone skilled in the art would so conclude. Xoft's contention that the term "radioactive material" is indefinite because it contains no antecedent basis is without merit. Xoft offers no authority suggesting that the antecedent basis of a term used in a dependent claim must be stated in identical words.⁷ The court, therefore construes "the radioactive material" in claim 8 to be the "radionuclide(s)" referred to in claim 1.

<i>Claim Language</i>	<i>Court's Construction</i>
"The radioactive material"	The material of claim 1 containing a radionuclide.

"A plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
A plurality of radioactive solid particles placed at pre-determined locations within the inner spatial volume to provide a desired dose profile that is the sum of the radiation profiles of the plurality of particles.	Static array of solid radioactive particles each placed in a single location and mounted on distal ends of separate wires. Desired composite radiation profile" is indefinite.

Claim 12 of the patent is directed to "[t]he apparatus as in claim 1 wherein the material containing a radionuclide comprises a plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile." Xoft argues claim 12 is indefinite on two grounds: first, that "desired composite radiation profile" is not

⁷ At the *Markman* hearing, Xoft stated that it would provide a citation to such supporting authority. Tr. at 64. Xoft, however, has not done so.

1 defined, and second, that "inner spatial volume" is indefinite because no physical structure bounds it.
 2 The court rejects Xoft's second argument for the reasons given when construing "inner spatial
 3 volume" above. The court rejects Xoft's first argument because it presents no evidence that one
 4 skilled in the art would not understand "desired composite radiation profile."⁸ Cytac's proposed
 5 construction does not clarify the meaning of claim 12. However, since the language is
 6 understandable as is, no construction of "a plurality of radioactive solid particles placed at
 7 predetermined locations within the inner spatial volume to provide a desired composite radiation
 8 profile" is necessary or appropriate.

<i>Claim Language</i>	<i>Court's Construction</i>
"A plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile"	(no construction needed)

B. Terms of the '204 patent

15 Claim 1 of the '204 patent is similar to claim 1 of the '813 patent. Claim 1 of the '204
 16 patent describes:
 17

An interstitial brachytherapy apparatus for delivering radioactive emissions to an
 18 internal body location comprising:

- 19 (a) a catheter body member having a proximal end and distal end;
- 20 (b) an inner spatial volume disposed proximate to the distal end of the catheter
 body member;
- 21 (c) an outer spatial volume defined by an expandable surface element
 disposed proximate to the distal end of the body member in a surrounding
 relation to the inner spatial volume; and
- 22 (d) a radiation source disposed in the inner spatial volume and generating a
 three-dimensional isodose profile that is substantially similar in shape to the
 expandable surface element.

28 ⁸ It would seem that for one skilled in the art, it would be a relatively simple matter to add up the individual radiation profiles of individual particles. *See* Tr. at 75-76.

1 **"Interstitial"**

Cytec's proposed construction	Xoft's proposed construction
(no construction required)	Site in natural or surgically created cavity in body.

4 **"Brachytherapy"**

Cytec's proposed construction	Xoft's proposed construction
Radiation therapy delivered by a spatially confined radiation source at or near the site of the diseased tissue.	Radiation therapy delivered by a spatially confined radionuclide at or near a tumor or other proliferative tissue disease site.

8 **"Interstitial brachytherapy"**

Cytec's proposed construction	Xoft's proposed construction
Brachytherapy applied directly to the interspaces of a body tissue, where the interspaces are not naturally occurring.	Radiation therapy delivered by a spatially confined radionuclide at or near a tumor site in a natural or surgically created cavity in a body.

12 Cytec argues that "interstitial" and "brachytherapy" should be construed together;
 13 Xoft seeks a separate construction for each word. Cytec also complains that Xoft seeks to
 14 limit "brachytherapy" to radionuclides, arguing that the definition should encompass any
 15 radiation source. However, the patent provides a clear definition of "brachytherapy": "The
 16 term 'brachytherapy,' as used herein, refers to radiation therapy delivered by a spatially
 17 confined radioactive material inserted into the body at or near a tumor or other proliferative
 18 tissue disease site." '204 patent, col. 1, ll. 30-33. Here, the patentee clearly acted as his own
 19 lexicographer, and Cytec's arguments for a broader definition do not acknowledge this clear
 20 definition. The court construes "brachytherapy" to mean "radiation therapy delivered by a
 21 spatially-confined radioactive material inserted into the body at or near a tumor or other
 22 proliferative tissue disease site."⁹

23 Xoft argues that "interstitial" means any body cavity, while Cytec argues that
 24 "interstitial" should be limited to only non-naturally-occurring cavities. As Xoft points out,
 25 one medical dictionary defines "interstitial" as "1. Placed or lying between. 2. Pert. to

27 ⁹ This definition does not resolve the parties' dispute over whether "radioactive material" should be
 28 read to encompass only "radionuclides" (as Xoft wishes) or any "radiation source" (as Cytec urges).
 As the parties have separately sought construction of "radioactive material," the court will address
 construction of that phrase below.

1 interstices or spaces within an organ or tissue." TABER'S CYCLOPEDIC MEDICAL
 2 DICTIONARY, 1007 (Clayton M. Thomas, ed., 17th ed. 1993). Although not cited by the
 3 parties, a British oncology text indicates that "interstitial" has a particular meaning in the
 4 field of the invention:

5 Two main techniques are used for the delivery of radiation which is given
 6 either as an external beam or as short range radiation from an implanted radioactive
 7 source. External beam radiation usually involves megavoltage produced by linear
 8 accelerator as photons or electrons or from cobalt sources in the form of relative low
 9 energy X-rays or gamma rays. The latter are often used to treat relatively superficial
 10 lesions such as basal cell carcinoma or recurrences within the skin. High energy
 11 radiation can be used to treat deeply located lesions such as prostatic carcinomas
 without delivering an excessive dose to adjacent normal tissue. . . .

12 Interstitial implant irradiation gives a high local dose to the tumour and
 13 usually employs sources such as radium, iridium, or caesium used in the form of
 14 needles or wires implanted in the tumour. This technique is widely used in the
 15 treatment of head and neck cancers to deliver a high tumour dose without irradiation
 16 to sensitive organs such as the lens of the eye or the spinal cord.

17 I.S. Fentiman, *The local Treatment of Cancer*, INTRODUCTION TO THE CELLULAR & MOLECULAR
 18 BIOLOGY OF CANCER, 434, 446 (L.M. Franks & N.M. Teich, eds., 2d ed. 1991).

19 However, Cytc points out that regardless of any generally-accepted meaning of "interstitial"
 20 in the field of the invention, the patentee limited "interstitial" during prosecution to refer to only
 21 surgically-created cavities (and similarly defined "intercavital" to refer to natural body cavities):

22 Turning to the cited prior art, the Ishiwara device comprises a
 23 thermotherapeutic apparatus having a catheter body member, an inner lumen
 24 surrounded by an outer lumen, and a radiation source contained within the inner
 25 lumen. . . . Ishiwara's apparatus is inserted into a body cavity. Hence, the apparatus
 26 does not provide *interstitial* radiation treatment, as Applicant's invention requires, but
 rather intercavital radiation treatment.

27 Su Decl. (dkt. # 49), Ex. C (Amendment & Resp.) at 11 (citations omitted). This is consistent with
 28 the background section of the patent, which mentions surgical cavities several times but not natural
 ones. '204 patent, col. 1, ll. 19, 23, 25, 63, col. 2, l. 1. Also, although the summary section does not
 specify what type of cavities the apparatus claims are directed to, the summary makes clear that the
 method claims are directed to a method that "includes surgically creating access to the proliferating
 tissue within a patient and surgically resecting at least a portion of the proliferating tissue to create a
 resection cavity within body tissue." *Id.*, col. 3, ll. 3-6.

1 The parties did not brief the issue of how much weight the court should afford the
 2 prosecution history in this instance.¹⁰ The Federal Circuit has instructed that "[a]lthough prosecution
 3 history can be a useful tool for interpreting claim terms, it cannot be used to limit the scope of a
 4 claim unless the applicant took a position before the PTO that would lead a competitor to believe
 5 that the applicant had disavowed coverage of the relevant subject matter." *Schwing GmbH v.*
 6 *Putzmeister Aktiengesellschaft*, 305 F.3d 1318, 1324 (Fed. Cir. 2002). Here, the patentee clearly
 7 disavowed coverage of intercavitary radiation treatment when arguing to the PTO. Given the

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13¹⁰ In its recent *en banc* explanation of the evidence to be used in construing claims, the Federal
 14 Circuit devoted a paragraph to prosecution history:

15 In addition to consulting the specification, we have held that a court "should
 16 also consider the patent's prosecution history, if it is in evidence." *Markman*, 52 F.3d
 17 at 980; *see also Graham v. John Deere Co.*, 383 U.S. 1, 33, 86 S.Ct. 684, 15 L.Ed.2d
 18 545 (1966) ("[A]n invention is construed not only in the light of the claims, but also
 19 with reference to the file wrapper or prosecution history in the Patent Office."). The
 20 prosecution history, which we have designated as part of the "intrinsic evidence,"
 21 consists of the complete record of the proceedings before the PTO and includes the
 22 prior art cited during the examination of the patent. *Autogiro*, 384 F.2d at 399. Like
 23 the specification, the prosecution history provides evidence of how the PTO and the
 24 inventor understood the patent. *See Lemelson v. Gen. Mills, Inc.*, 968 F.2d 1202,
 25 1206 (Fed. Cir. 1992). Furthermore, like the specification, the prosecution history
 26 was created by the patentee in attempting to explain and obtain the patent. Yet
 27 because the prosecution history represents an ongoing negotiation between the PTO
 28 and the applicant, rather than the final product of that negotiation, it often lacks the
 clarity of the specification and thus is less useful for claim construction purposes.
See Inverness Med. Switz. GmbH v. Warner Lambert Co., 309 F.3d 1373, 1380-82
(Fed. Cir. 2002) (the ambiguity of the prosecution history made it less relevant to
claim construction); *Athletic Alternatives, Inc. v. Prince Mfg., Inc.*, 73 F.3d 1573,
1580 (Fed. Cir. 1996) (the ambiguity of the prosecution history made it "unhelpful as
an interpretive resource" for claim construction). Nonetheless, the prosecution
history can often inform the meaning of the claim language by demonstrating how the
inventor understood the invention and whether the inventor limited the invention in
the course of prosecution, making the claim scope narrower than it would otherwise
be. *Vitronics*, 90 F.3d at 1582-83; *see also Chimie v. PPG Indus., Inc.*, 402 F.3d
1371, 1384 (Fed. Cir. 2005) ("The purpose of consulting the prosecution history in
construing a claim is to 'exclude any interpretation that was disclaimed during
prosecution.'"), quoting *ZMI Corp. v. Cardiac Resuscitator Corp.*, 844 F.2d 1576,
1580 (Fed. Cir. 1988); *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576
(Fed. Cir. 1995).

Phillips v. AWH Corp., 415 F.3d 1303, 1317 (Fed. Cir. 2005) (*en banc*).

1 intrinsic evidence is of primary importance¹¹ and all supports Cytac's position, the court construes
 2 "interstitial" to mean "involving a surgically-created cavity in a body."

3 In light of the constructions of "interstitial" and "brachytherapy" above, no further
 4 construction of "interstitial brachytherapy" is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"interstitial"	involving a surgically-created cavity in a body
"brachytherapy"	radiation therapy delivered by a spatially-confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site
"interstitial brachytherapy"	(no construction necessary)

"Inner spatial volume"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
A region of space surrounded by an outer spatial volume that is defined by an expandable surface element	Inner balloon in two-balloon device or spherical solid radionuclide in one-balloon device.

11 The phrase "inner spatial volume" appears in both patents-in-suit. The parties' arguments
 12 regarding the meaning of "inner spatial volume" are similar for each patent. The relevant portions of
 13 the specification are the same, and, additionally, the '204 patent purports to incorporate by reference
 14 the '813 patent. '204 patent, col. 1, ll. 10-11. The court will therefore construe "inner spatial
 15 volume" in the '204 patent in the same manner as for the '813 patent.

<i>Claim Language</i>	<i>Court's Construction</i>
"inner spatial volume"	a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere.

11 The extrinsic evidence that Cytac used "intercavitory" in literature and advertising in a manner that encompasses the definitions of "interstitial" and "intercavitory" it advances now, *see Tr. at 93*, is of little weight in this situation. Similarly, evidence presented by Cytac that Xoft represented to the FDA that the term "interstitial" "is a more appropriate word for a cavity that is surgically created as compared to a natural body cavity," (*see Decl. of Henry Su Supp. Cytac's Supplemental Claim Construction Br., Ex. A*, is not entitled to significant weight although it does suggest that one skilled in the art construes the term as Cytac proposes.

"Outer spatial volume"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required) <i>or</i> A region of space defined by an expandable surface element and surrounding an inner spatial volume.	Balloon or cage.

The phrase "outer spatial volume" in the '204 patent is analogous to the "outer, closed, inflatable chamber" of the '813 patent. The "outer spatial volume" is also explained in a similar manner; it is "defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume." '204 patent, col. 8, ll. 22-25. Xoft again confuses the concepts of a volume with the boundary of a volume. Cytyc's proposed construction is congruent with the language of claim 1 of the '204 patent, so the court will construe "outer spatial volume" as "a region of space defined by an expandable surface element and surrounding an inner spatial volume."

<i>Claim Language</i>	<i>Court's Construction</i>
"outer spatial volume"	a region of space defined by an expandable surface element and surrounding an inner spatial volume

"Expandable surface element"

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required) <i>or</i> A device that can be expanded or inflated, such as an expandable cage or an inflatable balloon.	Deflated balloon or collapsed cage.

Xoft's basic argument is that "expandable surface element" must be a deflated structure because once something is fully inflated, it is no longer expandable. Xoft also points out that part (d) of claim 1 refers to the "isodose profile" being "substantially similar in shape to the expandable surface element" without specifying whether the expandable surface element is fully expanded. It is apparent that the patentee intended "expandable surface element" to refer to a structure whether it was fully inflated or not. Xoft's proposed construction would have this element wink out of

1 existence at full inflation, leaving the "outer spatial volume" unbounded and giving the "isodose
 2 profile" no shape. The court agrees with Cytac that no construction of the term is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"expandable surface element"	(no construction needed)

6 **"Radiation source"**

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	radionuclide

9 The patent provides a clear definition of "brachytherapy": "The term 'brachytherapy,' as used
 10 herein, refers to radiation therapy delivered by a spatially confined radioactive material inserted into
 11 the body at or near a tumor or other proliferative tissue disease site." All asserted independent
 12 claims of the '204 patent contain the phrase "interstitial brachytherapy," which the court has
 13 construed as "radiation therapy delivered by a spatially-confined radioactive material inserted into
 14 the body at or near a tumor or other proliferative tissue disease site." Cytac's argument that
 15 "radiation source" should not be construed to exclude any radiation sources must be rejected; the
 16 claims clearly do not contemplate a radiation source other than "radioactive material."

17 There is still, however, the question of whether "radioactive material" means the same thing
 18 as Xoft's proposed construction of "radionuclide."¹² In describing the preferred embodiment, the
 19 patent says: "[t]he inner volume **30** is then filled with a material containing a predetermined
 20 radionuclide, for example, I-125, I-131, Yb-169 or other source of radiation, such as radionuclides
 21 that emit photons, beta particles, gamma radiation, or other therapeutic rays." '204 patent, col. 4,
 22 ll. 9-13 (emphasis added). Since all the examples of sources of radiation given in the specification
 23 are radionuclides, the patentee appears to have intended to define "radioactive material" as
 24 "radionuclides." Cytac argued at the *Markman* hearing that "or other therapeutic rays" could refer to
 25 other sources such as x-rays. The words "or other therapeutic rays," however, clearly refers to types

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 27
 28 ¹² The parties have agreed that "radionuclide" means "an isotope that undergoes radioactive decay."

1 of radionuclides. Cytac's construction would require the patentee to have inserted the word "or"
 2 before "gamma radiation," indicating the end of the list of types of radionuclides.¹³

3 Dictionary definitions are consistent with construing "radiation source" as a "radionuclide."
 4 One definition of "radioactive" is "[a] descriptive term for a material made up of atoms in which
 5 radioactivity occurs." AMERICAN HERITAGE NEW DICTIONARY OF CULTURAL LITERACY (3d ed.
 6 2006). A medical dictionary provided by Xoft defines "radioactive" as "giving off radiation as the
 7 result of the disintegration of the nucleus of an atom." MOSBY'S MEDICAL, NURSING, AND ALLIED
 8 HEALTH DICTIONARY, 1326 (Kenneth N. Anderson *et al.* eds., 4th ed. 1994). Cytac has not
 9 presented evidence that one skilled in this art would understand "radioactive material" any
 10 differently. The court agrees with Xoft—the term "radioactive" in the context of the '204 patent
 11 does not encompass such radiation sources as x-ray tubes, and "radiation source" therefore should be
 12 taken to mean "radionuclide."

<i>Claim Language</i>	<i>Court's Construction</i>
"radiation source"	radionuclide

"Minimum prescribed dose"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
Minimum prescribed dose received within a target tissue for delivering therapeutic effects.	Minimum dose needed to treat cancer cells.

20 The parties have requested construction of the phrase "minimum prescribed dose" and point
 21 out that the term appears in claims 2, 18, 24, 32, and 36 of the '204 patent. The parties do not argue
 22 that the term should be construed differently for different claims. However, claims 2, 24, 32, and 36
 23 contain the phrase "minimum prescribed absorbed dose," and claim 18 contains the phrase
 24 "prescribed absorbed dose." These inconsistencies seem irrelevant, however, because the parties'
 25

26 ¹³ Cytac also stated that this was an "Oxford comma" issue. Tr. at 137-38. However, in the
 27 sentence at issue, the Oxford comma is the one after "gamma radiation." Whether it is present does
 28 not alter the meaning of the sentence. Cytac also argued that "we're in the land of eats, shoots and
 leaves." If Cytac was referring to a book of such title, the court does not see how that would support
 Cytac's argument; the theme of *Eats, Shoots & Leaves: The Zero Tolerance Approach to Punctuation* (2004).

dispute is whether any such doses should be limited to treatment of cancer cells or allowed to cover any potential therapeutic effects. The court's construction of "brachytherapy" limits the claims to treatments "at or near a tumor or other proliferative tissue disease site." Xoft's proposed construction is too narrow, and Cytac's is too broad. However, in light of the construction of "brachytherapy," no construction of "minimum prescribed dose" or similar phrases is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"minimum prescribed dose"	(no construction necessary)

"Delivering a prescribed absorbed dose"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

Xoft argues that the patent does not reveal how one goes about prescribing a dose using the device, and that the phrase "delivering a prescribed absorbed dose" is therefore fatally indefinite. The '204 patent, however, describes a tool for treating proliferative tissue disease. A patent could adequately describe and claim a new apparatus or method for making the corrective curves in contact lenses, but a description of the particular curves a patient might require would not be necessary. If those skilled in the art would know how to use the disclosed invention, describing how to use it is unnecessary—the patentee merely needs to adequately describe the invention. Since Xoft bears the burden of proving that those skilled in the art would not know how to use the tool or method described in the patent and has presented no evidence on the subject, the court rejects Xoft's contention that the phrase is indefinite. No construction is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"delivering a prescribed absorbed dose"	(no construction necessary)

"The inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
The inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering	(indefinite)

1 **"The inner and outer spatial volumes are configured to provide a minimum prescribed
2 absorbed dose"**

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
Configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue.	(indefinite)

3 The phrases "the inner and outer spatial volumes are configured to provide a minimum
4 prescribed absorbed dose" and "configuring the inner and outer spatial volumes to provide a
5 minimum prescribed absorbed dose" are not indefinite for essentially the same reasons given in the
6 previous section. As Cytyc again appears to be attempting to impermissibly broaden its claims to
7 capture any therapeutic effect, despite the clear limitation provided by the patentee's definition of
8 "brachytherapy," the court also cannot adopt Cytyc's proposed construction. No construction of the
9 disputed language is necessary in light of the court's construction of other terms in the patent.

<i>Claim Language</i>	<i>Court's Construction</i>
"the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"	(no construction necessary)
"the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"	(no construction necessary)

18 **"A minimum distance outward from the outer spatial volume expandable surface"**

<i>Cytyc's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

21 Claims 2, 24, 32, and 36 all include the phrase "the target tissue being defined between the
22 outer spatial volume expandable surface and a minimum distance outward from the outer spatial
23 volume expandable surface."¹⁴ Xoft asserts that "minimum distance" is indefinite in this context
24 because the patent does not explain how the minimum distance is determined.

27 ¹⁴ The court believes that one skilled in the art would understand that the patentee intended to define
28 "target tissue" as the tissue "between the outer spatial volume expandable surface and a minimum
 distance outward from the outer spatial volume expandable surface." Taken literally, the patent
 explains the physical location where the act of defining "target tissue" takes place.

1 Here, "minimum" does not appear to add anything to the patent. The "target tissue" is the
 2 tissue outside of the outer chamber for a fixed distance in all directions, but this fixed distance or
 3 how one determines it are not explained. It seems that one skilled in the art would know how to
 4 determine the distance. *See* Tr. at 85-89. But the patent may as well read "a short distance outward"
 5 or "a determined distance outward" or merely "a distance outward."

6 Cytac claims that specification provides some guidance and that the minimum distance may
 7 in some instances be between half and one centimeter. The specification does state that

8 device A can readily be configured to provide a dose in a therapeutic range, say
 9 between 40 to 60 Gray, at a distance between 0.5 and 1.0 cm from the outer spatial
 volume for an outer spatial volume having a diameter of 4.0 cm and being in contact
 with the resection cavity wall.

10 '204 patent, col. 6, ll. 31-35. However, Cytac neglects to mention that "device A" is "an interstitial
 11 brachytherapy apparatus . . . such as those employed in U.S. Pat. No. 5,429,582, having a single
 12 spatial volume **50** filled with a radioactive material in solution." '204 patent, col. 6, ll. 3-7. In any
 13 case, this discussion does not use the phrases "target tissue" or "a minimum distance outward."
 14 Nevertheless, Xoft has presented no evidence that one skilled in the art would not understand the
 15 phrase "the target tissue being defined between the outer spatial volume expandable surface and a
 16 minimum distance outward from the outer spatial volume expandable surface." Xoft has not met its
 17 burden of proving by clear and convincing evidence that this language is indefinite, and the court
 18 finds that no construction is necessary.

<i>Claim Language</i>	<i>Court's Construction</i>
"a minimum distance outward from the outer spatial volume expandable surface"	(no construction necessary)

22 **"Controlled dose"**

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

25 **"To reduce or prevent necrosis in healthy tissue proximate to the expandable surface"**

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required)	(indefinite)

1 **"Providing a controlled dose at the outer spatial volume expandable surface to reduce
2 or prevent necrosis in healthy tissue"**

<i>Cytec's proposed construction</i>	<i>Xoft's proposed construction</i>
Controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface	(indefinite)

7 Xoft argues that the patent does not reveal how one goes about controlling a dose using the
8 device and that "reducing necrosis" is a hopelessly vague concept, making the '204 patent indefinite.
9 Xoft, however, has presented no evidence that one skilled in the art would not be able to understand
10 the patent and has again failed to meet its burden of proof. The court will therefore adopt Cytec's
11 construction proposals. "Providing a controlled dose at the outer spatial volume expandable surface
12 to reduce or prevent necrosis in healthy tissue" means "controlling the ratio of the dose at the
13 expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the
14 target issue so that the dose at the expandable surface is not so high that it lethally damages cells in
15 healthy tissue in contact with the expandable surface."

<i>Claim Language</i>	<i>Court's Construction</i>
"controlled dose"	(no separate construction necessary)
"to reduce or prevent necrosis in healthy tissue proximate to the expandable surface"	(no separate construction necessary)
"providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue"	controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface

1 **"Adapting the expandable surface to contact tissue surrounding the resection cavity to**
 2 **conform the tissue"**

Cytyc's proposed construction	Xoft's proposed construction
(no construction required)	(indefinite)

4 Xoft's contention that this phrase is indefinite springs from its argument that "expandable
 5 surface element" means "deflated balloon or cage." As the court has rejected Xoft's interpretation of
 6 "expandable surface element," no construction of "adapting the expandable surface to contact tissue
 7 surrounding the resection cavity to conform the tissue" is necessary.

Claim Language	Court's Construction
"adapting the expandable surface to contact tissue surrounding the resection cavity to conform the tissue"	(no construction necessary)

12 **"Desired shape of the expandable surface element"**

Cytyc's proposed construction	Xoft's proposed construction
(no construction required)	(indefinite)

15 Xoft has again presented no evidence to back up an argument that the phrase is indefinite and
 16 therefore again fails to carry its burden of proof. No construction of "desired shape of the
 17 expandable surface element" is necessary.

Claim Language	Court's Construction
"desired shape of the expandable surface element"	(no construction necessary)

21 **"Predetermined spacing"**

Cytyc's proposed construction	Xoft's proposed construction
(no construction required)	(indefinite)

24 **"A predetermined spacing is provided between said inner spatial volume and the**
 25 **expandable surface element" / "A predetermined spacing between said inner spatial**
 25 **volume and the expandable surface element"**

Cytyc's proposed construction	Xoft's proposed construction
The distance between the inner spatial volume and the expandable surface element is determined in advance	(indefinite)

1 Xoft's contention that these phrases are indefinite is based on its argument that "expandable
 2 surface element" means "deflated balloon or cage," and Xoft has again presented no evidence to
 3 back up arguments that the phrases are indefinite. No construction of "predetermined spacing" is
 4 necessary. The court will adopt Cytac's proposals and define both of the long phrases ("a
 5 predetermined spacing is provided between said inner spatial volume and the expandable surface
 6 element" and "a predetermined spacing between said inner spatial volume and the expandable
 7 surface element") as "the distance between the inner spatial volume and the expandable surface
 8 element is determined in advance."

<i>Claim Language</i>	<i>Court's Construction</i>
"predetermined spacing"	(no construction necessary)
"a predetermined spacing is provided between said inner spatial volume and the expandable surface element" / "a predetermined spacing between said inner spatial volume and the expandable surface element"	the distance between the inner spatial volume and the expandable surface element is determined in advance

15 **"Intraoperatively"**

<i>Cytac's proposed construction</i>	<i>Xoft's proposed construction</i>
(no construction required) or During the surgical operation to remove proliferative tissue.	After surgical removal of tumor but prior to closing the surgical site

19 At the claim construction hearing, the parties appeared to agree on the definition of
 20 "interoperatively." See Tr. at 140. The previous apparent disagreement revolved around whether
 21 the surgical site could be closed before insertion of the catheter apparatus. The court understands
 22 that the parties agree that the catheter must be inserted before the surgical site is closed. The '204
 23 patent at column 7, lines 55-64, specifically refers to the catheter being inserted "[f]ollowing tumor
 24 resection, but prior to closing the surgical site."

<i>Claim Language</i>	<i>Court's Construction</i>
"intraoperatively"	following tumor resection, but prior to closing the surgical site

1 **"Solid radiation source"**

2 <i>Cytec's proposed construction</i>	3 <i>Xoft's proposed construction</i>
A radiation source that has a fixed shape and volume, and is not deformable	Solid radionuclide

4 The parties' primary dispute here is whether "radiation source" encompasses more than
 5 radionuclides, which the court addressed above to limit "radiation source" to radionuclides. Cytec
 6 presents a dictionary definition of "solid," namely, "of definite shape and volume; not liquid or
 7 gaseous," from the AMERICAN HERITAGE COLLEGE DICTIONARY, 1295 (3d ed. 1997). The court will
 8 therefore define "solid radiation source" as "a radionuclide of definite shape and volume; not liquid
 9 or gaseous."

10 <i>Claim Language</i>	11 <i>Court's Construction</i>
"solid radiation source"	a radionuclide of definite shape and volume; not liquid or gaseous

13 **"The prescribed absorbed dose is delivered to the target tissue in substantially three
 14 dimensions"**

15 <i>Cytec's proposed construction</i>	16 <i>Xoft's proposed construction</i>
The prescribed absorbed dose is delivered to the target tissue such that all points at a given outward distance from the tissue wall will receive the same dose.	(indefinite)

18 Xoft contends that "prescribed absorbed dose" and "in substantially three dimensions" render
 19 "the prescribed absorbed dose is delivered to the target tissue in substantially three dimensions"
 20 fatally indefinite. The court has already rejected Xoft's argument regarding "prescribed absorbed
 21 dose."

22 Xoft points to Cytec's expert's testimony that "there's no such thing as substantially three
 23 dimensions" because something is either three dimensional or not. Mulville Decl. (dkt. # 51), Ex. L
 24 (Verhey Decl.) at 153. Cytec points to Xoft's expert's testimony that he could envision a
 25 brachytherapy apparatus that delivered 99 percent of its radiation in a plane; Cytec claims such a flat
 26 radiation field would not be in substantially three dimensions. Though a closer question than some
 27 of Xoft's other indefiniteness contentions, the court nonetheless finds that Xoft has not shown by
 28 clear and convincing evidence that one skilled in the art would not understand "in substantially three

1 dimensions" in the manner put forth by Cytac. The court therefore adopts Cytac's proposed
 2 construction for "the prescribed absorbed dose is delivered to the target tissue in substantially three
 3 dimensions," namely, "the prescribed absorbed dose is delivered to the target tissue such that all
 4 points at a given outward distance from the tissue wall will receive the same dose."

<i>Claim Language</i>	<i>Court's Construction</i>
"the prescribed absorbed dose is delivered to the target tissue in substantially three dimensions"	the prescribed absorbed dose is delivered to the target tissue such that all points at a given outward distance from the tissue wall will receive the same dose

1

III. ORDER

2 1. For the reasons given above, the court adopts the following claim construction as detailed in
3 this order.

Term or phrase	Court's construction
"inner spatial volume"	a region of space surrounded by an outer spatial volume and either enclosed by a polymeric film wall or defined by the outside surface of a solid radionuclide sphere.
"outer, closed, inflatable chamber"	outer, closed, inflatable chamber
"predetermined constant spacing"	(no construction necessary)
"predetermined constant spacing between said inner spatial volume and radiation transparent wall"	spacing predetermined by one skilled in the art between the wall or edge of the inner spatial volume and the radiation transparent wall of the outer, closed, inflatable chamber, when inflated, which is constant in all directions if the outer chamber is spherical, or constant along a radial plane if the outer chamber is not spherical
"rendering uniform"	to make the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument
"Means . . . for rendering uniform the radial absorbed dose profile of the emissions"	Function: Making the absorbed dose of radiation more uniform to prevent over-treatment of body tissue at or close to the outer wall of the instrument. Structure: A radiation absorbing or attenuating material, <i>e.g.</i> , air, x-ray contrast fluid, contrast media used in angiography, water, a gas, or barium sulfate or their equivalents.
"The radioactive material"	The material of claim 1 containing a radionuclide.
"A plurality of radioactive solid particles placed at predetermined locations within the inner spatial volume to provide a desired composite radiation profile"	(no construction needed)
"interstitial"	involving a surgically-created cavity in a body
"brachytherapy"	radiation therapy delivered by a spatially-confined radioactive material inserted into the body at or near a tumor or other proliferative tissue disease site
"interstitial brachytherapy"	(no construction necessary)

United States District Court
 For the Northern District of California

1	"outer spatial volume"	a region of space defined by an expandable surface element and surrounding an inner "expandable surface element"(no construction needed)
2	"radiation source"	radionuclide
3	"minimum prescribed dose"	(no construction necessary)
4	"delivering a prescribed absorbed dose"	(no construction necessary)
5	"the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"	(no construction necessary)
6	"the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose"	(no construction necessary)
7	"a minimum distance outward from the outer spatial volume expandable surface"	(no construction necessary)
8	"controlled dose"	(no separate construction necessary)
9	"to reduce or prevent necrosis in healthy tissue proximate to the expandable surface"	(no separate construction necessary)
10	"providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue"	controlling the ratio of the dose at the expandable surface of the outer spatial volume to the prescribed dose at the depth of interest in the target issue so that the dose at the expandable surface is not so high that it lethally damages cells in healthy tissue in contact with the expandable surface
11	"adapting the expandable surface to contact tissue surrounding the resection cavity to conform the tissue"	(no construction necessary)
12	"desired shape of the expandable surface element"	(no construction necessary)
13	"predetermined spacing"	(no construction necessary)
14	"a predetermined spacing is provided between said inner spatial volume and the expandable surface element" / "a predetermined spacing between said inner spatial volume and the expandable surface element"	the distance between the inner spatial volume and the expandable surface element is determined in advance
15	"intraoperatively"	following tumor resection, but prior to closing the surgical site
16	"solid radiation source"	a radionuclide of definite shape and volume; not liquid or gaseous
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1 "the prescribed absorbed dose is delivered to
2 the target tissue in substantially three
3 dimensions"

the prescribed absorbed dose is delivered to the
target tissue such that all points at a given
outward distance from the tissue wall will
receive the same dose

4 2. The parties shall appear for a further case management conference on June 1, 2007 at 10:30
5 a.m. and shall file a further joint case management conference statement no later than four
6 days prior.

7
8 DATED: 4/27/07

Ronald M Whyte
9 RONALD M. WHYTE
United States District Judge
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9 registered for e-filing under the court's CM/ECF program.

10
11 **Dated:** 4/27/07

12

SPT
13 Chambers of Judge Whyte
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11 UNITED STATES DISTRICT COURT
12 NORTHERN DISTRICT OF CALIFORNIA
13 SAN JOSE DIVISION

14 HOLOGIC, INC., CYTYC CORPORATION,
and HOLOGIC L.P.,

15 Plaintiffs,

16 vs.

17 SENORX, INC.,

18 Defendant.

19 Case No. C08 00133 RMW (RS)

20 **DECLARATION OF LYNN J. VERHEY,
Ph.D. IN SUPPORT OF PLAINTIFFS'
PROPOSED CONSTRUCTION OF CLAIM
TERMS, PHRASES AND CLAUSES**

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28 AND RELATED COUNTERCLAIMS.

1 I, Lynn J. Verhey, Ph.D., declare and state as follows:

2 I have been retained in this case as an expert witness by Plaintiffs Hologic, Inc., Cytac
 3 Corporation, and Hologic L.P (“Hologic”). I make this declaration based on my personal knowledge,
 4 training and experience, and if I were to be called to testify, I could and would testify competently
 5 about the subject matter set forth below.

6 I understand that the parties propose different constructions of various terms, phrases and
 7 clauses in the patents-in-suit. I submit this declaration to provide my opinion on the meaning of the
 8 disputed claim terms.

9 **I. INTRODUCTION AND MY EXPERT QUALIFICATIONS**

10 On April 3, 2008, in support of Hologic’s Motion for Preliminary Injunction, I submitted a
 11 declaration describing my current employment and summarizing my background and education. Ex. A
 12 (¶¶ 3-7) (Dkt. No. 77). I have also submitted a current curriculum vitae to the Court. Ex. B. In the
 13 April 3, 2008 declaration, I explained that I previously served as an expert witness for Cytac
 14 Corporation (Cytac has since been acquired by Hologic) in the case of *Xoft, Inc. v. Cytac Corporation*
 15 and *Proxima Therapeutics, Inc.*, Case No. C05-05312 RMW (¶ 8) (the “Xoft litigation”). The Xoft
 16 litigation involved United States Patent Nos. 5,913,813 (the “‘813 patent”) and 6,413,204 (the “‘204
 17 patent”), both of which are at issue in this case.¹ In that declaration, I also briefly described the subject
 18 matter of the three patents-in-suit. Ex. A at ¶ 9. Rather than repeating those statements again, I
 19 incorporate the contents of my April 3, 2008 declaration by reference.

20 **II. TOPICS THAT I HAVE BEEN ASKED TO ADDRESS**

21 I have been asked to provide opinions regarding how a person of ordinary skill in the art would
 22 interpret the meaning of certain claim terms and phrases from the ‘813, ‘204 and ‘142 patents.

23 **III. INFORMATION CONSIDERED IN FORMING MY OPINIONS**

24 On October 12, 2006, I submitted a declaration in the prior Xoft litigation relating to claim
 25 construction issues in that case. Ex. C. A substantial part of that declaration is relevant to the present

27 ¹ A third patent, United States Patent No. 6,482,142 (the “‘142 patent”), is also at issue in this case.

1 case. Rather than repeating those statements again, I incorporate the contents of my October 12, 2006
 2 declaration by reference. Ex. C. Therein, I identified the information I considered in forming my
 3 claim construction opinions. *Id.* at 2-3. I have considered the same information here, with the
 4 following additions: (1) I have reviewed and considered the text of the '142 patent and the file history
 5 associated with its issuance; (2) I have reviewed and followed the claim constructions that the Court
 6 issued in the Xoft case for the '813 and '204 patents; and (3) I have reviewed and considered the claim
 7 constructions proposed by the parties in this case. I have not reviewed any written or oral opinions
 8 from any expert whom SenoRx has retained or may retain in connection with this case. I reserve the
 9 right to modify my opinions stated in this declaration after having reviewed any such opinion offered
 10 by any such expert. I also reserve the right to modify my opinions based on any rulings that the Court
 11 might issue in the future relating to these patents.

12 **IV. APPROACH I HAVE USED IN READING THE '813, '204, AND '142 PATENTS AND
 13 INTERPRETING THEIR CLAIMS**

14 In my October 12, 2006 declaration (Ex. C), I explained my methodology for interpreting claim
 15 terms and phrases from the '813 and '204 patents. The statements made in that declaration with regard
 16 to my approach to claim construction apply equally to the present case.

17 This case involves one additional patent and different asserted claims. I understand that the
 18 claims of the '813 patent at issue in this lawsuit are claims 11 and 12, found in columns 5 and 6 of the
 19 patent. I understand that the claims of the '204 patent at issue here are claims 4 and 17, found in
 20 columns 8 and 9 of the patent. I understand that the claims of the '142 patent at issue here are claims
 21 1, 6 and 8, found in columns 8, 9, and 10 of the patent. I understand that all three patents are related to
 22 one another by lineage, with the '813 patent being the parent. The '204 and '142 patents are
 23 continuations-in-part of the '813 patent.

24 **V. LEVEL OF SKILL OF ONE OF ORDINARY SKILL IN THE ART**

25 In my October 12, 2006 declaration (Ex. C), I identified the skill level of one of ordinary skill
 26 in the art for purposes of interpreting the claims of the '813 and '204 patents. *Id.* at 4. The same skill
 27 level would apply to construing the '142 patent claims.

1 **VI. THE MEANING OF THE DISPUTED CLAIM TERMS IN THE ‘813, ‘204, AND ‘142
2 PATENTS**

3 I have reviewed and relied upon the material identified in Section III above. Based on these
4 materials, my knowledge and experience in the technical field to which the patented inventions relate,
5 and my familiarity with the level of ordinary skill in the art at the times the applications for the ‘813,
6 ‘204, and ‘142 patents were filed, I have formed opinions as to how one of ordinary skill in the art
7 would have interpreted certain claim terms at the time of their invention. My opinion regarding the
8 meaning of each of the disputed claim terms is set forth below. Where the disputed term is present in
9 more than one of the asserted patents, my interpretation is given only once. The list of disputed terms
10 includes those identified by either party. For a few of the terms, I provide an explanation of why I
11 disagree with SenoRx’s proposed construction.

12 **VII. TERMS ALREADY CONSTRUED IN THE PRIOR XOFT LITIGATION**

13 I notice that SenoRx disputes a number of claim terms that the Court already construed in the
14 prior Xoft litigation. I will not address those terms already construed by the Court. I reserve the right
15 to address them at a later point in time if appropriate.

16 **The ‘813 Patent**

17 “inner spatial volume” (claims 1, 2, and 12) - The Court previously construed this term to
18 mean “a region of space surrounded by an outer spatial volume and either enclosed by a polymeric
19 film wall or defined by the outside surface of a solid radionuclide.” Col. 1:50-2:3; 2:33-63; 3:9-16, 42-
20 48; 3:64-4:12; 4:16-30, 32-52; 6:6-7; Figs. 1, 3-5; Decl. of Katharine Altemus in Support of Plaintiffs’
21 Opening Claim Construction Brief (“Altemus Decl.”) at 3-5, 28 (Claim Construction Order from *Xoft,*
22 *Inc. v. Cytac Corp. et al.*) I address this term again only to respond to a particular problem I see with
23 SenoRx’s proposed construction.

24 SenoRx proposes to modify the Court’s construction to limit, for embodiments where the
25 “inner spatial volume” is defined by the outside surface of a solid radionuclide, the radionuclide to a
26 “sphere.” This is an artificially narrow construction, which does not accurately reflect standard
27 brachytherapy treatment. One skilled in the art of brachytherapy would know that in a typical
28 brachytherapy procedure using a solid radionuclide, the radionuclide is not necessarily spherical in

1 shape and does not need to be. This was also true in 1997, when the application for the ‘813 patent
2 was filed. Therefore, to so limit the definition of the term “inner spatial volume” does not accurately
3 reflect standard practice. Nor does it comport with the claim language, which does not include or
4 imply such limiting language.

5 “inner, closed chamber” (claim 2) – One of ordinary skill in the art would understand this term
6 as written – i.e., it means “inner, closed chamber.” No further elaboration or explanation is needed.

7 It does not make sense from a technical standpoint to say that the inner spatial volume must be
8 “completely” inside the outer chamber or “closed off within the outer chamber,” as SenoRx suggests.
9 Clearly, as seen in the text of the ‘813 patent, Col. 2:36-38, and as commonly understood in the field,
10 an inner spatial volume that is an inner, closed chamber defined by a radiation transparent wall must
11 still permit a radiation source to be placed in there. If it were completely sealed or closed off, that
12 would not be possible.

The ‘204 Patent

“three-dimensional isodose profile that is substantially similar in shape to the expandable surface element” (claim 1) – means exactly that, “three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.” One of ordinary skill in the art would understand this term as written. No further elaboration or explanation is needed.

“plurality of solid radiation sources” (claim 17) – means exactly that, “plurality of solid radiation sources.” One of ordinary skill in the art would understand this term as written. No further elaboration or explanation is needed.

21 “isodose profile having a shape substantially similar to the shape of the outer spatial volume”
22 (claim 17) – means exactly that, “isodose profile having a shape substantially similar to the shape of
23 the outer spatial volume.” One of ordinary skill in the art would understand this term as written. No
24 further elaboration or explanation is needed.

The ‘142 Patent

26 “three-dimensional apparatus volume configured to fill an interstitial void” (claims 1 and 8) –
27 In my opinion, this claim phrase can only be understood in the context of the limitation in which it

1 appears and is a part of. This limitation is “an expandable outer surface *defining* a three-dimensional
 2 apparatus volume *configured to fill* an interstitial void created by the surgical extraction of diseased
 3 tissue *and define* an inner boundary of the target tissue being treated.” As the italicized language
 4 makes clear, the “three-dimensional apparatus volume” is something that is defined by the “expandable
 5 outer surface.” What this expandable outer surface defines is a three-dimensional geometric solid
 6 (e.g., a sphere) having both volume that fills an interstitial void created by the surgical extraction of
 7 diseased tissue and a surface area that defines an inner boundary of the target tissue being treated.
 8 Accordingly, in my opinion, the term “three-dimensional apparatus volume” means “a three-
 9 dimensional geometric solid composed of an expandable outer surface.” By “solid,” I mean a
 10 geometric shape, such as a sphere, having three dimensions and a surface area.

11 In my opinion, SenoRx construes this claim term divorced from its context. I agree that the
 12 patentee’s use of the word “volume” here is somewhat unusual. However, it is clear from the context
 13 that the patentee uses the term “apparatus volume” to refer to a three-dimensional geometric solid or
 14 shape defined by the expandable outer surface rather than “a region of space within the expandable
 15 outer surface” – as SenoRx’s suggests. Col. 2:20-53, 60-64; 3:20-36, 55-62, 66-67; 4:1-2, 27-42; 5:36-
 16 65; 6:11-29; 8:1-32, 52-59, Figs. 1, 3-4.

17 “located so as to be spaced apart from the apparatus volume” (claim 1) – Like the preceding
 18 claim phrase, this claim phrase can only be understood in the context of the limitation in which it
 19 appears and is a part of. This limitation is “a radiation source disposed completely within the
 20 expandable outer surface and located so as to be spaced apart from the apparatus volume.” As noted
 21 above, the three-dimensional apparatus volume is a geometric solid defined by the expandable outer
 22 surface that has both volume and surface area. Understood in this context, the phrase “located so as to
 23 be spaced apart from the apparatus volume” logically refers to the surface area of the apparatus volume
 24 that defines the inner boundary of the target tissue being treated. Accordingly, in my opinion, this
 25 claim phrase means “located so as to be not on or touching the apparatus volume.” Col. 2:20-53; 3:20-
 26 25, 55-62, 66-67; 4:1-2, 27-30, 35-57; 5:36-65; 6:11-29; 7:1-15, 49-55; 8:1-32, 52-59; Figs. 1, 3-4.

27 \\

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“asymmetrically located and arranged within the expandable surface” (claim 1) – means “located and arranged so as not to be on the longitudinal axis of the expandable surface.” Col 2:20-53; 3:7-19, 55-62, 66-67; 4:1-2; 5:12-37; 6:11-29, 24-67; 7:1-15; 8:1-32, 52-59; Figs. 1, 3-4.

4 "predetermined asymmetric isodose curves" (claims 1, 6 and 8) – means "predetermined
5 isodose curves that are not symmetric with respect to the longitudinal axis of the apparatus volume."
6 Col. 2:20-53; 2:60-3:1; 3:7-19; 5:12-37; 6:11-29, 24-67; 7:28-48; 7:62-8:32; 8:52-59.

“plurality of solid radiation sources” (claim 6) – means exactly that, “plurality of solid radiation sources.” One of ordinary skill in the art would understand this term as written. No further elaboration or explanation is needed.

10 “being provided on at least two elongate members extending into the apparatus volume” (claim
11 6) – means exactly that, “being provided on at least two elongate members extending into the
12 apparatus volume.” One of ordinary skill in the art would understand this term as written. As
13 explained above, the three-dimensional apparatus volume defined by the expandable outer surface is a
14 geometric solid that has both volume and surface area. In the context of this limitation, it is clear the
15 two elongate members are extending into the volume of this geometric solid.

16 I declare that the foregoing is true and correct to the best of my knowledge under penalty of
17 perjury.

18 Executed on May 21, 2008 in San Francisco, California.

Lynn J. Verhey, Ph.D.

Exhibit A

Case 5:08-cv-00133-RMW Document 35-8 Filed 04/02/2008 Page 2 of 6
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16 Attorneys for Plaintiffs

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18 UNITED STATES DISTRICT COURT
19 NORTHERN DISTRICT OF CALIFORNIA
20 SAN JOSE DIVISION

21 HOLOGIC, INC., CYTYC CORPORATION,
22 and HOLOGIC L.P.,

23 Plaintiffs,

24 vs.

25 SENORX, INC.,

26 Defendant.

27 Case No. C08 00133 RMW (RS)

28 **DECLARATION OF LYNN J. VERHEY,
Ph.D. IN SUPPORT OF PLAINTIFFS'
MOTION FOR PRELIMINARY
INJUNCTION**

Date: April 21, 2008

Time: 2:00 p.m.

Room: Courtroom 6, 4th Floor

Judge: Hon. Ronald M. Whyte

29 AND RELATED COUNTERCLAIMS.

1. I have been retained in this case as an expert witness by Plaintiffs Hologic, Inc., Cytoc
2 Corporation, and Hologic L.P. I make this declaration based on my personal knowledge, training and
3 experience, and if I were to be called to testify, I could and would testify competently about the subject
4 matter set forth below.

5 2. I am presently employed by the University of California, San Francisco, as a Full
6 Professor and I serve as Vice-Chair in the Department of Radiation Oncology. Attached to this
7 declaration as Exhibit A is a copy of my curriculum vitae.

8 3. To briefly summarize my background and education, I received my B.A. in Physics
9 from Kalamazoo College, Kalamazoo, Michigan in 1962, and my M.S. and Ph.D. in Physics in 1964
10 and 1968, respectively, from the University of Illinois, Urbana, Illinois. The subject of my research
11 during my education was on the decays of certain charged particles produced by high energy
12 interactions of protons with Hydrogen and Deuterium.

13 4. After earning my doctorate, I took a position at UCLA and served as a post-doctoral
14 researcher and Assistant Professor of Physics from 1968-70, doing experiments at Lawrence Berkeley
15 Laboratory and teaching physics to undergraduate physics students. I then moved to Harvard
16 University in 1970 as an Assistant Professor, continuing to teach undergraduate physics and perform
17 high energy experiments, this time at Fermi National Laboratory in Illinois.

18 5. In 1975 I took a position as Hospital Radiation Physicist at Massachusetts General
19 Hospital (MGH) with a concurrent continuing position as Assistant Professor at the Harvard Medical
20 School. I then worked with the MGH group to develop and implement proton radiation therapy as an
21 alternative to x-ray therapy.

22 6. In 1990, I took the position as Chief of the Physics Division and Associate Professor in
23 the Department of Radiation Oncology at UCSF. Since that time, I have continued to serve as Physics
24 Chief and, in addition, as Vice-Chair of the Department and as a Full Professor. As part of my
25 responsibilities at UCSF, I have mentored numerous graduate and post-graduate students, taught
26 graduate classes in the Department of Bioengineering at the University of California, Berkeley as well
27

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as at UCSF. I have taught medical physics to medical residents at UCSF as well as to physics residents. I have performed research on methods of delivering radiation to cancer patients and have published over 100 technical papers in this field.

7. I was certified as a therapeutic radiological physicist by the American Board of Radiology in 1982, appointed a fellow of the American Association of Physicists in Medicine in 2002 and a fellow of the American Society of Therapeutic Radiology and Oncology in 2006. I am a well-recognized expert in methods of delivering radiation to cancer patients, having given numerous scientific lectures and scientific meetings, both nationally and internationally.

8. I previously served as an expert witness for Cytac Corporation in the case of *Xoft, Inc. v. Cytac Corporation and Proxima Therapeutics, Inc.*, Case No. C05-05312 RMW, which was also pending in this Court. I understand that this case, like the *Xoft* case, involves claims of infringement of United States Patent Nos. 5,913,813 (the "813 patent") and 6,413,204 (the "204 patent"). I also understand that a third United States Patent, No. 6,482,142 (the "142 patent"), is involved in this case as well.

9. In general, the 813 patent describes and claims an invention in the field of a balloon catheter for treatment of proliferative tissue, while the 204 patent extends this concept to describe and claim as an invention a method for treatment of proliferative tissue diseases using an interstitial brachytherapy apparatus. These patents describe a catheter which can be used with an array of radiation-producing materials to irradiate the wall of a surgical cavity and a defined thickness of tissue beyond that wall, to doses that can both avoid necrosis of normal tissue and destroy cancer cells that might populate the area. The 142 patent further extends the concept of the 813 patent to describe and claim balloon catheter devices that are capable of delivering asymmetrically shaped radiation doses.

10. In connection with my role as an expert witness in the *Xoft* case, I offered this Court the following definition of a person of ordinary skill in the art, which is applicable here as well given that the same family of patents is at issue. In understanding what is taught and claimed in the 813, 204 and 142 patents, the relevant scientific area is radiation oncology physics, with a focus on brachytherapy. Typically, individuals of ordinary skill in the art of this field would hold an M.S. degree in Physics or

11. Such a person would have a broad knowledge of the physics of brachytherapy
procedures, of the principles of radioactivity and an understanding of the effects of radiation on cells.
In addition, such a person would have an understanding of other means of treating cancer cells with
radiation such as an external, gantry-mounted linear accelerator. Individuals with such qualifications
are considered eligible for certification as a radiation oncology physicist by entities such as the
American Board of Radiology and considered capable of working independently in a clinical
environment as a medical physicist.

12. I have been asked by Plaintiffs' counsel to describe, from the viewpoint of a person of
ordinary skill in the art (as defined above), what is disclosed and taught in two technical documents:
(1) a 1990 article entitled "A New Technique of Brachytherapy for Malignant Gliomas with Cesium-
137: A New Method Utilizing a remote Afterloading System," by Ashpole et al. (attached as Ex. 5 to
the Declaration of Aaron P. Maurer) ("Ashpole"), and (2) U.S. Patent No. 5,931,774 to Williams, et al.
(attached as Ex. 13 to the Declaration of Aaron P. Maurer) (the "774 patent"), entitled "Inflatable
Devices for Tumor Treatment" which describes "implantable devices for treatment of proliferative
disorders." I have been provided with copies of both documents and have reviewed them.

13. Ashpole describes the irradiation of a cavity from which a brain tumor has been
removed, using an intracranial applicator made by modifying an endotracheal tube. In its unmodified
form, the endotracheal tube has an open lumen that provides an unobstructed airway and an inflatable
balloon, called a cuff, attached near its distal end that seals the space between the tube and the trachea
to prevent the aspiration of unwanted matter from the pharynx into the trachea. To be used as an
intracranial applicator, the endotracheal tube is shortened in length and sealed off at its distal end, just
beyond the lower end of the balloon. Page 334, column 1.

14. The intracranial applicator is visually inserted into the postsurgical cavity following the
removal of the brain tumor, and the balloon is then inflated with a radio-opaque fluid (needed for
treatment planning purposes) so that it approximately fills the cavity. The volume of fluid used varies

15. There is no teaching in Ashpole that the balloon can be expanded to conform the shape
of the cavity to the outer surface of the balloon, or that the balloon comes into contact with the tumor
bed at all points, or that the distance from the tumor bed to the radiation source can be adjusted through
expansion of the balloon. Indeed, one of ordinary skill in the art would understand that undue
deformation and compression of sensitive normal brain tissue caused by the influx of an
incompressible fluid, are not desirable.

16. After the intracranial applicator has been implanted, it is attached to a Selectron remote
afterloader, which pushes dummy sources into the tube, using positions which represent potential
dwelling points for the radioactive sources during treatment. Ashpole produces a desired mean dose
rate at a given distance from the balloon's surface by varying the position of active and inactive beads
in the source train until an isodose curve is found, which is a satisfactory match to the cavity shape. In
other words, the desired dose distribution is a direct result of the particular arrangement of active and
inactive beads on a source train, and Ashpole aims to compute an isodose surface that conforms to the
particular shape of the postsurgical cavity, rather than reshaping the cavity to conform to the outer
surface of the balloon. Page 336, column 1 ("A certain measure of dosimetric versatility is possible
in that the positions of the active beads can be changed to produce an isodose distribution specific to
the geometry of the individual tumor beds.").

17. In Ashpole the configuration of the balloon plays a role only to ensure that the dose at
the prescribed depth of 0.5 cm is greater than 50% of that at the surface of the balloon. To ensure the
minimum ratio, Ashpole teaches that "the balloon diameter should not be less than 2.5 cm." Page 336,
column 2. Ashpole does not teach changing the balloon diameter after implantation. Rather, it
prescribes a minimum diameter to which a balloon should be inflated with radio-opaque fluid during
implantation.

18. Ashpole does not disclose controlling the dose at the surface of the balloon so that it is
not so high that it lethally damages healthy brain cells in contact with the surface. For instance, it

1 indicates that “[t]he dose at the surface of the balloon . . . can be as high as 70 Gy,” notwithstanding
2 the fact that “the limited tolerance of normal brain has restricted the maximum permissible dose to
3 about 55-60 Gy.” Page 333, column 2; page 336, column 2. Furthermore, if one applies the inverse
4 square law to Ashpole’s “typical case [of] a balloon diameter of 2.9 cm,” then a depth dose of 50Gy at
5 0.5 cm from the surface of the balloon would mean a dose of approximately 90 Gy at the surface,
6 assuming a symmetric distribution of sources within the balloon. Ashpole’s teaching of a minimum
7 balloon diameter of 2.5 cm suggests that for a dose of 50Gy at 0.5 cm from the cavity surface, that the
8 dose at the surface can be even higher than 90 Gy.

9 19. Ashpole explains that the intracranial applicator avoids the problem of late or delayed
10 radionecrosis observed with the use of long-term wire implants because the intracranial applicator is
11 removable and implanted into an area from which the tumor has already been debulked. Page 336,
12 column 2.

13 20. The 774 patent discloses an implantable balloon applicator for delivering one or more
14 treatment fluids to target tissue. Although it discusses several embodiments, the one of particular
15 interest is a “double balloon device” with an outer and inner balloon, as depicted in Figure 3.

16 21. The 774 patent teaches that “it is preferable that the balloon have a shape that permits
17 the balloon to conform to the body cavity or lumen in which the balloon is to be inflated.” Column 7,
18 lines 41-43. Furthermore, “[i]n certain embodiments, a balloon will be selected such that, upon
19 inflation, the balloon does not compress the tissue which is being treated, or surrounding tissues. Thus,
20 when a radioactive treatment fluid is introduced into the device, e.g., by injection, the treatment device
21 is inflated to a volume not substantially greater than a volume of the body cavity in which the device
22 has been placed, thereby avoiding any substantial compression or distortion of normal tissue.” Column
23 7, lines 48-56. This is consistent with the disclosure in Ashpole, in which the applicator balloon,
24 because it is being used within the brain, is inflated with fluid to a volume only sufficient to fill the
25 postsurgical cavity in which the device has been placed but not to cause any compression or
26 deformation of the surrounding brain tissue.

27
28

2 receptacles, one in communication with the outer balloon and the other one in communication with the
3 inner balloon. Column 8, lines 41-46 and 54-60. The outer balloon in this example is filled with a
4 chemotherapeutic fluid and the inner balloon is filled with a radioactive fluid. Column 8, lines 60-65.

5 23. Although Figure 3 shows the inner balloon as having an off-center position relative to
6 the outer balloon, this is a schematic view only and not something drawn to scale. Column 3, lines 1-
7 2. Accordingly, the degree to which the inner balloon occupies an asymmetric position relative to the
8 outer balloon, which is not mentioned or discussed at all in the 774 patent, cannot be determined. It
9 would depend on the device's actual design and construction.

10 24. More importantly, neither Figure 3 nor the specification of the 774 patent teaches a
11 person of ordinary skill in the art how the radiation source in the inner balloon can be *located and*
12 *arranged* to provide *predetermined* asymmetric isodose curves relative to the outer balloon. If the
13 inner balloon has an asymmetry relative to the outer balloon, that asymmetry is fixed by the geometric
14 constraints of the device, and therefore the position of the inner balloon cannot be altered to provide
15 predetermined asymmetric isodose. Instead, any asymmetric dose distribution produced by the
16 radioactive fluid in the inner balloon would be a byproduct of the inner balloon's inherent asymmetry.

17 25. In addition to the *Xoft* case mentioned above, for which I provided both deposition and
18 hearing testimony, I provided testimony as an expert at a deposition in the case of *Maggiani vs.*
19 *University of Southern California* conducted on February 20, 2006.

20 26. I am being compensated for my work on this matter at a rate of \$500 per hour. My
21 compensation does not depend on the outcome of this case.

22 I declare that the foregoing is true and correct to the best of my knowledge under penalty of
23 perjury.

24 Executed on April 3 , 2008 in San Francisco, California.


Lynn J. Verhey, Ph.D.

Exhibit B

Lynn J. Verhey, PhD

University of California, San Francisco**Updated: 5/10/07****CURRICULUM VITAE****Name:** **Lynn J. Verhey**

Position: Professor in Residence, Step 6
 Department of Radiation Oncology
 School of Medicine

Faculty Member, Bioengineering Graduate Group

Address: UCSF Comprehensive Cancer Center
 Suite H-1031, Box 1708
 San Francisco, CA 94143-1708

Voice: (415) 353-7184
 FAX: (415) 353-7182
 email: verhey@radonc17.ucsf.edu

EDUCATION:

1958-62	Kalamazoo College, Kalamazoo, MI	BA	Physics, Cum Laude
1962-64	University of Illinois, Urbana, IL	MS	Physics
1964-67	University of Illinois, Urbana, IL	PhD	Physics

BOARD CERTIFICATION:

1982 American Board of Radiology (Therapeutic Radiological Physics)

PRINCIPAL POSITIONS HELD:

1967-70	University of California, LA	Assistant Professor	Physics
1971-72	Harvard University	Lecturer	Physics
1972-75	Harvard University	Assistant Professor	Physics
1975-90	Harvard Medical School	Assistant Professor	Radiation Therapy
1991-96	University of California, SF	Assoc. Professor in Residence	Radiation Oncology
1996-now	University of California, SF	Professor in Residence	Radiation Oncology

OTHER POSITIONS HELD CONCURRENTLY:

1975-78	Massachusetts General Hospital	Assistant Biophysicist	Radiation Medicine
1978-90	Massachusetts General Hospital	Associate Biophysicist	Radiation Medicine
1978-90	Massachusetts General Hospital	Head, Clinical Physics	Proton Therapy

Lynn J. Verhey, PhD

1991-now	University of California, SF	Chief of Physics	Radiation Oncology
1991-now	University of California, SF	Vice-Chair	Radiation Oncology
1991-00	University of California, SF	Faculty	Graduate Group in Biophysics
1994-now	UCSF and UC Berkeley	Faculty	Bioengineering Graduate Group

HONORS AND AWARDS:

1962 Phi Beta Kappa, Kalamazoo College
 1962 John Wesley Hornbeck Prize in Physics, Kalamazoo College, Kalamazoo, MI
 2002 Fellow, American Association of Physicists in Medicine
 2006 Fellow, American Society of Therapeutic Radiation and Oncology

KEYWORDS/AREAS OF INTEREST:

Radiotherapy, intensity modulation, protons, radiosurgery, ocular melanoma, dosimetry, image-guided radiotherapy, magnetic resonance spectroscopy, cancer of the prostate, head and neck and brain.

PROFESSIONAL ACTIVITIES**CLINICAL:**

Head of clinical physics from 1978-90 for the proton radiation treatment program of the Department of Radiation Therapy, Massachusetts General Hospital.

Director of Physics for Gamma Knife Facility, University of California, San Francisco since 1991

Director of Physics for ocular melanoma proton treatment facility University of California, San Francisco and University of California, Davis since 1994

Implementation and direction of intensity modulated radiotherapy treatments at UCSF since 1997

Specification and oversight for acquisition, installation, commissioning and operation of \$20 million state-of-the-art Radiation Oncology Department at UCSF Comprehensive Cancer Center at Mount Zion from 1998 to present

SUMMARY OF CLINICAL ACTIVITIES

As Chief of Physics in the Department of Radiation Oncology at UCSF, I am responsible for all technical aspects of the planning and delivery of sophisticated precision radiotherapy and radiosurgery. This includes supervision and oversight of approximately 20 radiation therapists, six dosimetrists, two engineers and eight physicists. I provide oversight and direction to the physics faculty in their clinical service and in the development of new clinical delivery schemes and imaging methods. As Director of Physics for the Gamma Knife, I coordinate and oversee quality assurance of treatments, safety and radiation training of all personnel, new upgrades of software and hardware and the installation of new radiation sources.

PROFESSIONAL ORGANIZATIONS:

Memberships

1962	Phi Beta Kappa
1966	Sigma Pi Sigma
1975-80	American Association of Physics Teachers
1976-now	American Association of Physicists in Medicine
1979-now	American Society of Therapeutic Radiologists
1979-99	Radiation Research Society
1983-90	American Association for the Advancement of Science
1984-now	Proton Therapy Cooperative Group
1986-90	New York Academy of Science
1992-now	International Stereotactic Radiosurgery Society
1995-now	California Radiological Society
1995-now	American College of Radiology

Service to Professional Organizations

1991-97	Chairman of Quality Assurance Committee of Proton Radiation Oncology Group Sponsored by American College of Radiology
1992-99	Member, RTOG Committee on Quality Assurance in Conformal Radiation Therapy (3D-CRT)
1992-97	Member, Radiation Physics Committee of American Society for Therapeutic Radiology and Oncology (ASTRO)
1992-93	Member, Research Committee, American Association of Physicists in Medicine (AAPM)
1993-95	Reviewer for Awards and Honors Committee of AAPM
1993-now	Reviewer of abstracts for Annual meeting of AAPM
1993-03	Reviewer of abstracts for Annual Meeting of ASTRO
1994	Reviewer of abstracts for 1994 Annual Meeting of the Radiological Society of North America (RSNA)
1995-now	Member, Committee on Quality Assurance for Cooperative Clinical Trials, a Subcommittee of the Radiation Therapy Committee of the AAPM
1996-01	Member, Committee on Membership of ASTRO
1996-01	Member, 3D Committee of the Radiation Therapy Oncology Group (RTOG)
2000-02	Member, Awards Committee of ASTRO
2003-now	Member, Corporate Working Group of ASTRO

SERVICE TO PROFESSIONAL PUBLICATIONS

1998-now	Editorial Board, International Journal Radiation Oncology, Biology and Physics (IJROBP)
1988-now	Ad hoc referee for IJROBP (10 papers in past 5 years), Medical Physics (5 papers in past 5 years), British Journal of Radiology (2 papers in past 5 years), Radiotherapy and Oncology (2 papers in past 5 years), Physics in Medicine and Biology (8 papers in past 5 years)

INVITED PRESENTATIONS (PAST 15 YEARS)

INTERNATIONAL

1991 International Workshop on Heavy Charged Particle Therapy and Related Subjects, National Institute for Radiological Sciences, Chiba, Japan

1991 World Congress on Medical Physics and Biomedical Engineering, Kyoto, Japan

1993 International Leksell Gamma Knife Society Meeting, Aronsborg, Sweden

1993 International Symposium on 3D Radiation Treatment Planning and Conformal Therapy, St. Louis, MO

1994 Proton Therapy Cooperative Group Meeting, Chester, England

1994 Proton Therapy Cooperative Group Meeting, Chiba, Japan

1995 Siemens Vision Group on New Directions in Radiotherapy, Frankfurt, Germany

1995 Annual Meeting of the International Commission on Radiation Units and Measurements (ICRU) in Remscheid-Lennep, Germany

1995 US-Japan Radiation Oncology Meeting, San Francisco, CA

1995 International Stereotactic Radiosurgery Meeting, Boston, MA

1997 XII International Conference on the Use of Computers in Radiation Therapy, Salt Lake City, Utah

1997 First Professor S. Takahashi Memorial International Workshop on Three Dimensional Conformal Radiotherapy, Nagoya, Japan

1997 Siemens Therapy Products Enduser Meeting and Seminar, Beijing, China

1997 International Congress of Radiation Oncology, Beijing, China

1997 Third Congress of the International Stereotactic Radiosurgery Society, Madrid, Spain

1997 ESTRO Workshop on Challenges in Conformal Radiotherapy, Nice, France

1998 DKFZ (Deutsche Krebs Forschung Zentrum), Heidelberg, Germany

1998 3rd International Symposium on 3-D Radiation Treatment Planning and Conformal Radiotherapy, Chapel Hill, NC

1998 Second Professor S. Takahashi Memorial International Workshop on Three Dimensional Conformal Radiotherapy, Nagoya, Japan

1999 International Stereotactic Radiosurgery Society (ISRS) Meeting, Sydney, Australia

1999 Annual Meting of Societe Francaise De Radiotherapie Oncologique, Paris, France

2000 2nd Annual Wharton Lecture, Princess Margaret Hospital, Toronto, Canada

2000 Hallym Hospital, Seoul, Korea

2000 Samsung Hospital, Seoul, Korea

2000 Addenbrookes Hospital, Cambridge, England

2000 Annual Meeting of the European Society for Therapeutic Radiology and Oncology (ESTRO), Istanbul, Turkey

2000 First International Symposium on Stereotactically Guided IMRS/IMRT, Los Angeles, CA

2001 International Congress on Radiation Oncology (ICRO), Melbourne, Australia

2001 Sun-Yat-Sen Cancer Center, Taipei, Taiwan

2001 Third Professor S. Takahashi Memorial International Workshop on Three Dimensional Conformal Radiotherapy, Nagoya, Japan

2002 Leksell Gamma Knife Society Meeting, Prague, Czech Republic

2002 Hospital Sirio Libanes, Sao Paulo, Brazil

Lynn J. Verhey, PhD

2002 Joint Meeting Canadian Organization of Medical Physicists and American Association of Medical Physicists, Montreal, Canada

2003 NZIMRT Annual Conference, Hamilton, New Zealand

2003 Organizer, Moderator and Speaker, 7th International Conference on 3DCRT/IMRT, San Francisco, CA

2003 2nd International Conference on Translational Research and Pre-Clinical Strategies in Radio-Oncology, Lugano, Switzerland

2004 Fourth Professor S. Takahashi Memorial International Workshop on Three Dimensional Conformal Radiotherapy, Nagoya, Japan

NATIONAL

1992 Special Focus Panel at Annual Meeting of Radiological Society of North America, Chicago, IL:

1993 Special Panel on Conformal Therapy at the Annual Meeting of the American Society for Therapeutic Radiation and Oncology, New Orleans, LA

1994 Preuss Foundation Seminar on Stereotactic Radiation Treatment of Brain Tumors, Boston MA

1995 Special Workshop at the Annual Meeting of the Radiation Research Society on "New Methods of Delivering Radiation Therapy", San Jose, CA

1995 Symposium on Implementation of Emergent Technology in Radiation Oncology, Indian Wells, CA

1995 Scientific Session of the Radiation Therapy Oncology Group Annual Meeting, Philadelphia, PA

1996 Workshop on Intensity Modulated Radiation Therapy, Durango, CO

1996 Radiation Therapy Oncology Group Annual Meeting, Washington, DC

1997 Visiting Professor, Duke University Medical Center, Department of Radiation Oncology Grand Rounds, Durham, NC

1997 14th Annual Meeting of the American College of Medical Physics, Lake Tahoe, CA

1998 20th Annual Engineering Industrial Liaison Program, University of Calif., Berkeley, CA

1998 Intensity Modulated Radiation Therapy Workshop, Williamsburg, VA

1998 Annual Meeting of the American Association of Physicists in Medicine (AAPM), San Antonio, TX

1999 Radiation Therapy Oncology Group (RTOG) Annual Meeting, Atlanta, GA

1999 3-D Meeting on Conformal and Intensity Modulated Radiation Therapy, Houston, TX

1999 Annual Meeting of AAPM, Nashville, TN

1999 National Cancer Institute Workshop on Medical Physics for Clinical Radiotherapy, Washington, DC

1999 Annual Meeting of the American Association of Therapeutic Radiology and Oncology (ASTRO), San Antonio, TX

2000 3-D Conformal Radiotherapy Workshop, New York, NY

2000 Combined Meeting of World Congress of Medical Physicists and AAPM, Chicago, IL

2000 Annual Meeting of ASTRO, Boston, MA

2000 Siemens Users' Meeting, Kiawah Island, SC

2001 International Stereotactic Radiosurgery Society (ISRS), Las Vegas, NM

2001 Annual Meeting of AAPM, Salt Lake City, UT

Lynn J. Verhey, PhD

2001 Visiting Professor, Symposium Honoring the Career of Dr. Michael Goitein at Massachusetts General Hospital, Boston, MA
 2002 Visiting Professor, Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA
 2002 Annual Meeting of ASTRO, New Orleans, LA
 2003 Annual Meeting of ASTRO, Salt Lake City, UT
 2003 Organizer, Moderator and Speaker, Proton Therapy Cooperative Group Meeting, San Francisco, CA
 2003 Siemens Users' Meeting, Salt Lake City, UT
 2004 Annual Meeting of AAPM, Pittsburgh, PA
 2004 Annual Meeting of ASTRO, Atlanta, GA
 2004 Annual Meeting of American Association of Physics Teachers, Sacramento, CA

REGIONAL AND OTHER INVITED PRESENTATIONS

1991 Cancer Education Session, Stanford University Department of Radiation Oncology, Stanford, CA
 1993 Department of Physics, Sonoma State University, Rohnert Park, CA
 1993 Bay Area Chapter of the American Association of Neuroscience Nurses
 1994 Grand Rounds, Department of Radiation Oncology, UCSF
 1994 29th Annual San Francisco Cancer Symposium, San Francisco, CA
 1995 15th Annual Current Approaches to Radiation Oncology, Biology and Physics, San Francisco, CA
 1996 Northern California Society of Radiation Therapy Technologists, Concord, CA
 1997 16th Annual Current Approaches to Radiation Oncology, Biology and Physics, San Francisco, CA
 1997 Annual Retreat of the Graduate Group in Biophysics, UCSF, Tiburon, CA
 1998 17th Annual Current Approaches to Radiation Oncology, Biology and Physics, San Francisco, CA
 1999 18th Annual Current Approaches to Radiation Oncology, Biology and Physics, San Francisco, CA
 1999 First Annual Radiosurgery Symposium, UCSF
 2001 Stanford University IMRT Symposium, Palo Alto, CA
 2002 Cyberknife Users' Meeting, Napa, CA
 2002 Siemens Users' Meeting, Santa Rosa, CA
 2002 UCSF-Stanford Post-Graduate Course – Scientific Program Coordinator and Moderator
 2002 Joint Meeting of SFSU-UCSF U56 Collaborative Advisory Committee
 2003 UCSF-Stanford Post-Graduate Course – Scientific Program Coordinator and Moderator

GOVERNMENT AND OTHER PROFESSIONAL SERVICE:

1990-97 Chair, Report Committee on Proton Therapy, International Commission on Radiation Units and Measurements (ICRU)
 1990-91 Loma Linda University Medical Center: Safety Review Committee on the Proton Therapy Facility
 1992-93 Lawrence Berkeley Laboratory, University of California, Berkeley: Dosimetry Review Committee for Heavy Ion Radiotherapy Program

Lynn J. Verhey, PhD

1992 Lawrence Berkeley Laboratory, University of California, Berkeley: Research Medicine and Radiation Biophysics Division Review Committee

1992-93 National Cancer Institute: Program Project Scientific Review Panel

1993 National Cancer Institute: Review Committee for Radiological Physics Center at M.D. Anderson Hospital, Houston, TX

1993-95 Nuclear Regulatory Commission and Lawrence Livermore National Laboratory: Reviewer of Quality Management Plans

1995 TRIUMF and the British Columbia Cancer Agency: Safety Review Committee on the Proton Therapy Facility

1996 National Cancer Institute: Member, Special Review Committee for Program Project at University of Michigan Medical Center

1997-04 Takahashi International Workshop Organizing Committee, Nagoya, Japan

1997-01 National Cancer Institute: Member, Special Ad Hoc Review Committee of the Radiation Studies Section of NCI

1999 External Physics Consultant to Swedish Hospital, Seattle, WA

1999 External Advisor to University of Texas Medical Branch, Galveston, TX

1999-01 National Cancer Institute: Member, Intensity Modulated Radiotherapy Cooperative Working Group

2000 National Cancer Institute: Member, Special Review Committee for Program Project at University of Michigan Medical Center

2000-03 Cancer Research Coordinating Committee of State of California: Reviewer of Research Proposals

2001 Special Advisor to Department of Radiation Oncology, Princess Margaret Hospital, Toronto, Canada

2004 Special Ad Hoc Reviewer of Research Proposal for the Dutch Cancer Society

UNIVERSITY AND PUBLIC SERVICE

UNIVERSITY SERVICE:

UCSF, UC BERKELEY AND UC DAVIS CAMPUS-WIDE

1991-00 Faculty member of the Graduate Group in Biophysics, University of California, San Francisco

1991-93 Member, University of California, Davis Cancer Center Proton Beam Task Force and Clinical Specifications Subcommittee

1992-03 Chair, Radiation Drug Research Committee, University of California, San Francisco

1992-03 Member, Radiation Safety Committee, University of California, San Francisco

1993-95 Member, Environmental Health and Sciences Advisory Group, University of California, San Francisco

1994 Chair, Ad Hoc Promotion Review Committee, University of California, San Francisco

1994 Founding Member, UCSF Cancer Center

1994-now Faculty member of Bioengineering Graduate Program, University of California, Berkeley

1997-00 Member, Health and Safety Policy Board of the University of California, San Francisco

1998,99,02 Member Ad Hoc Promotion Review Committees, University of California, San Francisco

1998 Vice-Chair, Admissions Committee of the Bioengineering Graduate Program, University of California, Berkeley

1998-now Specification and oversight for acquisition, installation, commissioning and operation of \$20 M state-of-the-art Radiation Oncology Department at UCSF Comprehensive Cancer Center at Mount Zion

1999 Chair, Admissions Committee of the Bioengineering Graduate Program, University of California, Berkeley

2000-03 Member, Graduate Council of the Academic Senate, University of California, San Francisco

2001-now Member, UCSF Health and Safety Policy Board

2001-03 Member, Bioengineering Graduate Group Executive Committee

2001-02 Member, Academic Senate Subcommittee on Creation of a UCSF School of Advanced Health Studies

2003-now Member, Bioengineering Graduate Group Advisors' Committee

2002-03 Service on Qualifying and Final Exam Committees for Bioengineering Grad. Students

2004- Member, Educational Policy Committee of the Academic Senate, UCSF

DEPARTMENTAL SERVICE

1991-now Vice Chair and Chief of Physics

1991-now Member, Internal Computer Committee

1991-now Member, External Computer Committee

1991-now Member, Program Committee of Annual Course on Current Approaches to Radiation Oncology, Biology and Physics

Lynn J. Verhey, PhD

1991-94	Member, Mt. Zion -University of California, San Francisco Radiation Oncology Integration Committee
1991-now	Member, Quality Assurance / Quality Improvement Committee
1991-now	Member, Radiation Oncology Research Allocation Committee
1991-now	Member, Radiation Oncology Resident Selection Committee
1991-now	Member, Executive Committee of Department of Radiation Oncology
1993-94	Chair, Faculty Search Committee for Physics Faculty in Hyperthermia
1993-now	Initiator and Director, Physics Residency Training Program in Therapeutic Radiation Oncology Physics
1996	Member, Faculty Search Committee for Assistant Professor in Residence with Combined Research/Clinical Duties
1997	Chair, Ad Hoc Committee for Selection of NOMOS Medical Research Fellow for Clinical Implementation of Intensity Modulated Radiation Therapy
1997	Member, Faculty Search Committee for Wun-Kon Fu Endowed Chair in Radiation Oncology
1998	Member, Senior Promotions Committee
1998	Chair, Ad Hoc Committee for Selection of Siemens Medical Research Fellow
1998	Chair, Faculty Search Committee for Assistant Professor in Residence (Physics)
2001-now	Member, Radiation Oncology Animal Care Review Committee

PUBLIC SERVICE:

1990	Member of scientific delegation for US-Soviet Union Proton Therapy Exchange Program
1993-98	Member, Medical Physics Advisory Committee (MEDPAC), Lawrence Livermore National Laboratory
1998	Scientific American Interview with W. Wayt Gibbs
1998	Wired Magazine Interview with Heidi Kriz
2000-03	Scientific Advisory Board, Accuray, Inc.
2001-04	Scientific Advisory Board, MED-TEC, Inc.

SUMMARY OF SERVICE ACTIVITIES

Most of my service activities in the past five years have been associated with administrative duties within the Department of Radiation Oncology, campus-wide committees, and activities within the cross-campus Bioengineering Graduate Group, where I am an active faculty member. As a member of the executive committee of the Department of Radiation Oncology, I am involved in all decisions relating to finances, promotions and salaries, and space allocation. As the Chief of the Physics Division within the department, I have special mentoring and advising duties for the other physics faculty as well as technical supervision of engineers, dosimetrists and radiation therapists. As Director of the Physics Residency Training Program, I have major responsibilities to select, mentor and advise the residents in their clinical training program. As a member of the Medical Residency Selection Committee, I work with a small group of department faculty to interview and rank resident candidates. As a member of the Program Committee of the Annual UCSF-Stanford Post-Graduate Course on Current Approaches to Radiation Oncology, Biology and Physics, I am responsible for planning and arranging the physics and technical presentations. As a long-standing member of the Radiation

Lynn J. Verhey, PhD

Safety Committee of the campus until 2003, I was one of several members responsible for investigating and analyzing the use of radioactivity in research and in clinical activities. As a member of the Scientific Advisory Board of two vendors of medical equipment used in Radiation Oncology, I have been able to influence the development of devices that improve the quality of patient care.

TEACHING and MENTORING

FORMAL SCHEDULED CLASSES FOR UCSF AND UCB STUDENTS:

Qtr	Acad. Yr	Course No. & Title	Contribution	Units	Class Size
F,W	1998-99	Medicine 424 Therapeutic Radiological Physics	Lecturer	1	5
F,W	1999-00	Medicine 424 Therapeutic Radiological Physics	Lecturer	1	5
F,W	2000-01	Medicine 424 Therapeutic Radiological Physics	Lecturer	1	5
F,W	2001-02	Medicine 424 Therapeutic Radiological Physics	Lecturer	1	5
F,W	2002-03	Medicine 424 Therapeutic Radiological Physics	Lecturer	1	5
F,W	2003-04	Medicine 424 Therapeutic Radiological Physics	Lecturer	1	5
F	2000-01	NE 167 Engineering Aspects Nuc Med / RadioTherapy	Course Design and Lecturer	3	10
S	2001-02	Bioeng. 230C Physics of Radiation Oncology	Course Design and Lecturer	3	5
S	2003-04	Bioeng 230C Physics of Radiation Oncology	Course Design and Lecturer	3	8
S	2005-06	Bioeng 230C Physics of Radiation Oncology	Course Design and Lecturer	3	4

POSTGRADUATE AND OTHER COURSES

2003 7th International Conference on 3DCRT/IMRT, San Francisco, Organizer, Moderator and Speaker
 2002-05 UCSF-Stanford Post-Graduate Course on Radiation Oncology – Scientific Program Coordinator, Moderator and Speaker
 2002-06 Gamma Knife Model C training for outside clinicians and physicists

PREDCTORAL STUDENTS SUPERVISED OR MENTORED

Dates	Name	Program or School	Role	Current Position
1998-99	Nkiruka Emeagwali	Johns Hopkins	Research advisor	Graduate Student
1998-00	Gordon Wong	Bioengineering, UCB	Research advisor	Graduate Student
1999-02	Ted Graves	Bioengineering, UCSF	Research co-mentor	Asst. Prof. Stanford

2000	Andrew Hwang	Bioengineering, UCSF	Rotation coordinator	Graduate Student
2001-02	Richard Cardenas	Texas Tech University	Research co-mentor	Asst Prof St. Marys TX
2003-	Michael Lometti	SFSU MS student	Research co-mentor	Research Associate
2004-	Erica Ludlam	Bioengineering, UCSF	Research co-mentor	Graduate Student
2003-	Olivier Morin	Bioengineering, UCSF	Research co-mentor Academic advisor	Graduate Student
2002-04	Annette A. Chan	Bioengineering, UCSF	Research co-mentor Academic advisor	Post-doctoral Researcher
2004-	Cornelius VonMorze	Bioengineering, UCSF	Academic advisor	Graduate Student

POSTDOCTORAL FELLOWS AND RESIDENTS DIRECTLY SUPERVISED OR MENTORED

Dates	Name	Fellow/Resident	Faculty Role	Current Position
1992-95	Su-Min Zhou	Physics Res. Fellow	Research Advisor	Assoc. Prof. Duke
1993-95	Bruce Hill	Physics Resident	Clinical Training	Physicist - Stanford
1994-95	Tibor Major	IAEA Physics Fellow	Research Advisor	Physicist – Hungary
1994-98	Inder Daftari	Hospital Physicist	Clinical Training	Hospital Physicist UCSF
1994-96	Greg Bednarz	Physics Resident	Clinical Training	Physicist– U. Penn
1995-97	Ping Xia	Physics Resident	Clinical Training	Assoc. Prof. UCSF
1998-00	Michelle Svatos	Physics Res. Fellow	Research Advisor	Physicist - Siemens
1996-98	Jenny Hai	Physics Resident	Clinical Training	Physicist- Stanford
1997-99	D Jay Wieczorek	Physics Resident	Clinical Training	Physicist – Baptist Hosp. Miami
1998-00	Lei Wang	Physics Resident	Clinical Training	Asst Prof Sequoia Hosp
1999-02	Cynthia Chuang	Physics Resident	Clinical Training	Clin. Instructor UCSF
1999-01	Andrea Pirzkall	Research Fellow	Research Supervision	Asst. Adj. Prof. UCSF
2000-03	Katja Langen	Physics Resident	Clinical Training	Physicist – MD Anderson Orlando
2000-01	Khalil Sultanem	Clinical Fellow	Research Supervision	Attending Physician
2002-04	Jose-Eduardo Villarreal	Physics Resident	Clinical Training	Physicist - Mount Diablo Hospital
2001-02	Jean Nakamura	Rad. Onc. Resident	Research Supervision	Instructor, UCSF
2002-05	Ningsheng Zhu	Physics Resident	Clinical Training	Physics Resident
2003-07	Josephine Chen	Research Fellow and Physics Resident	Research and Clinical Training	Research Fellow and Resident

Lynn J. Verhey, PhD

2003-05	Hong Chen	Physics Resident	Clinical Training	Physics Resident
2005-07	Martina Descovich	Physics Resident	Clinical Training	Physics Resident
2007-09	Tarek Halabi	Physics Resident	Clinical Training	Physics Resident

RADIATION ONCOLOGY RESIDENTS AND FELLOWS – CLINICAL INSTRUCTION

1989-92	Marquez, Carol Bahary, Jean-Paul Uhl, Valerie Stalpers, Lucas Feehan, Patrick Gotkowitz, Carrie	Levin, Ken Garwood, Dan Miyawaki, Lloyd Eng, Tony Lillis, Patricia Chang, Garrick	Stalpers, Lucas Levine, Rene Schoenthaler, Robin Scharfen, Cindy Weil, Michael Hunter, Darryl
1992-95	Holland, John Goldsmith, Brian Diaz, Aidnag	Yates, Barbara Schrieve, Dennis Tran, Loan	Maloney, Alan Ling, Stella Schultz, Marion
1995-99	Crownover, Richard Haas-Kogan, Daphne Chou, Rachel Le, Quynh-Thu	Bermudez, Maria-Amelia Bauman, Glenn Chen, Anita Forstner, Julie	Koeplin, David Coleman, Lori Shu, Hui-Kuo Song, Joseph
1999-01	Seung, Steven Posner, Marc	Coleman, Cardella Gottschalk, Alex	Seaward, Samantha Hoffman, Rex
2001-03	Suplica, Jeffrey Fisch, Ben Sultanem, Khalil Nakamura, Jean Lee	Vigneault, Eric Lee, Terry Young, C. Dale Takamiya, Robert	Bertucio, Clare Tsao, May Biggs, Christopher Lowther, David
2003-present	Stickney, Eric Ho, Linh Missett, Brian Chen, Allen Lee, Brian	Doyle, Kelly Huang, David Coleman, Joy Dai, Charlotte	Huang, Kim Rembert, James Millender, Laura Hansen, Eric

INFORMAL TEACHING:

1991-07 Teaching Gamma Knife planning to residents, fellows and faculty
 1991-07 In-service lectures on radiosurgery, IMRT and clinical physics

FACULTY MENTORING

Dates	Name	Position while Mentored	Mentoring Role	Current Position
1994-96	Paula Petti	Asst. Professor	Academic and research advisor	Adjunct Professor UCSF
1998-02	Ping Xia	Clinical Instructor	Academic and research advisor, reviewed grant proposal	Associate Professor in Residence, UCSF
2002-now	Cynthia Chuang	Clinical Instructor	Academic and research advisor	Asst. Adjunct Professor, UCSF
2003	Bruce Faddegon	Associate Professor	Reviewed grant proposal	Associate Professor, UCSF
2001-04	Andrea Pirzkall	Assistant Researcher	Reviewed manuscripts, academic advisor	Associate Professor, UCSF
2006-07	Lijun Ma	Associate Professor	Reviewed manuscripts and mentored research	Associate Professor, UCSF

SUMMARY OF TEACHING HOURS:

2002-03 305 total hours of teaching (including preparation)
 Formal class or course teaching hours: 25 hours
 Informal teaching hours: 250 hours
 Mentoring: 30 hours

2003-04 390 total hours of teaching (including preparation)
 Formal class or course teaching hours: 80 hours
 Informal teaching hours: 280 hours
 Mentoring: 30 hours

2004-05 335 total hours of teaching (including preparation)
 Formal class or course teaching hours: 30 hours
 Informal teaching hours: 280 hours
 Mentoring: 25 hours

TEACHING NARRATIVE:

My teaching hours are divided between formal courses, including a quarter course (Bioengineering 230C) recently introduced by me to offer the Physics of Radiation Oncology as a subject. From this course, several graduate students have become interested in research in the physics of Radiation Oncology and are now doing rotations or beginning thesis research in our group. As director of the Physics Residency Training Program, I have been responsible for designing the curriculum, selecting the residents and assuring their progress through the clinical training. Two of the graduates of this program have stayed to become faculty in our Department. As Chief of Physics, I am responsible for the physics education of the medical residents. I have also taken responsibility for mentoring new faculty in the Physics Division as well as clinical physics instruction for new medical faculty. In summary, it is my responsibility to educate all faculty and staff in the physics of Radiation Oncology.

RESEARCH AND CREATIVE ACTIVITIES

RESEARCH AWARDS AND GRANTS

CURRENT

U56 Minority Institution/Cancer Center Partnership Cancer Training and Career Development NIH/NCI (PI: Macher)	04/01/02-03/31/07 \$2,500,000 direct
Siemens – UCSF Research Collaborative Agreement Research on Portal Imaging and Intensity Modulation Siemens Oncology Systems (PI: Verhey)	10/01/05-09/30/07 \$390,000 direct

PENDING

Radiosurgical Treatment of Temporal Lobe Epilepsy
NIH/NINDS (PI: Barbaro)

PAST

R01 NS39280 Radiosurgical Treatment of Temporal Lobe Epilepsy NIH/NINDS (PI: Barbaro)	09/30/00-08/31/03 \$266,481 direct
Award for Physics Residency Training Program ASTRO/AAPM (PI: Verhey)	09/01/96-08/31/98 \$30,000 direct

PEER REVIEWED PUBLICATIONS

1. Abrams RJ, Abashian A, Mischke RE, Nefkens BMK, Smith JH, Thatcher RC, Verhey LJ, Wattenberg A. Test of time reversal invariance in the decay $K_L^0 \rightarrow \pi^- \mu^+ \nu$. *Phys Rev Letters* 17:606-608, 1966.
2. Verhey LJ, Nefkens BMK, Abashian A, Abrams RJ, Carpenter DW, Mischke RE, Smith JH, Thatcher RC, Wattenberg A. Experimental investigation of CP violation in K_e^3 decays. *Phys Rev Letters* 17:669-671, 1966.
3. Mischke RE, Abashian A, Abrams RJ, Carpenter DW, Nefkens BMK, Smith JH, Thatcher RC, Verhey LJ, Wattenberg A. Determination of the phase of the CP-nonconservation parameter n_{\pm} in neutral K decay. *Phys Rev Letters* 18:138-141, 1967.
4. Thatcher RC, Abashian A, Abrams RJ, Carpenter DW, Mischke RE, Nefkens BMK, Smith JH, Verhey LJ, Wattenberg A. Upper limit on the decay rate $K_L^0 \rightarrow \pi^+ \pi^- \gamma$ *Phys Rev D* 4:1674-1680, 1968.
5. Abrams RJ, Abashian A, Mischke RE, Nefkens BMK, Smith JH, Thatcher RC, Verhey LJ, Wattenberg A. Muon polarization in K μ^3 meson decay. *Phys Rev D* 5:1603-1615, 1968.
6. Parsons ASL, Truoel P, Berardo PA, Haddock RP, Verhey LJ, Zeller ME. A scintillation counter array for detection of high energy neutrons. *Nuc Inst and Methods* 79:43-50, 1970.
7. Berardo PA, Haddock RP, Nefkens BMK, Verhey LJ, Zeller ME, Parsons ASL, Truoel P. Measurement of the $\pi^- p \rightarrow \gamma n$ differential cross section near the roper resonance, P_{11} (1460). *Phys Rev Letters* 24:419-422, 1970.
8. Berardo PA, Haddock RP, Nefkens BMK, Verhey LJ, Zeller ME, Parsons ASL, Truoel P. Measurement of inverse pion photoproduction near the P_{33}^0 (1236) resonance. *Phys Rev Letters* 26:201-204, 1971.
9. Berardo PA, Haddock RP, Helland J, Nefkens BMK, Verhey LJ, Zeller ME, Parsons ASL, Truoel P. Analysis of negative pion photoproduction near the P_{33} resonance: test of the $\Delta I \leq 1$ rule and T-reversal invariance. *Phys Rev Letters* 26:205-208, 1971.
10. Berardo PA, Haddock RP, Nefkens BMK, Verhey LJ, Zeller ME, Parsons ASL, Truoel P. A measurement of the differential cross-section $\pi^- p \rightarrow n \pi^0$. *Phys Rev D* 6:756-766, 1972.
11. Berardo PA, Haddock RP, Nefkens BMK, Verhey LJ, Zeller ME, Parsons ASL, Truoel P. Differential cross-sections of $\pi^- p \rightarrow \gamma n$ for 317, 452 and 491 MeV/c incident pion momentum. *Phys Rev D* 9:621-643, 1974.
12. Comiso JC, Blasberg DJ, Haddock RP, Nefkens BMK, Truoel P, Verhey LJ. Inverse pion photoproduction in the vicinity of the P_{33} (1232) resonance and a test of time reversal invariance. *Phys Rev D* 12:719-737, 1975.
13. Comiso JC, Blasberg DJ, Haddock RP, Nefkens BMK, Truoel P, Verhey LJ. Differential cross-section measurements of $\pi^- p \rightarrow \pi^0 n$ around the P_{33} (1232) resonance. *Phys. Rev. D* 12:738-743, 1975.
14. Loomis WA, Matis HS, Anderson HL, Bharadwaj VK, Booth NE, Fine RM, Francis WR, Gordon BA, Heisterberg RH, Hicks RG, Kirk TBW, Kirkbride GI, Mo LW, Myrianthopoulos LC, Pipkin RM, Pordes SH, Quirk SC. Inclusive hadron production in inelastic muon-proton scattering at 150 GeV/c. *Phys Rev Letters* 35:1483, 1975.

15. Weiss AJ, Blasberg DJ, Comiso JC, Haddock RP, Nefkens BMK, Verhey LJ, Zeller MB, Crowe KM, Fainberg A, Truoel P. Measurement of differential cross-sections for radiative pion-proton capture in the second resonance region. *Nuc Phys.* B101:1-18, 1975.
16. Anderson HL, Bharadwaj VK, Booth NE, Fine RM, Francis WR, Gordon BA, Heisterberg RH, Hicks RG, Kirk TBW, Kirkbride GI, Loomis WA, Matis HS, Mo LW, Myrianthopoulos LC, Pipkin FM, Pordes SH, Quirk SW, Shambroom WD, Skuja A, Verhey LJ, Williams WSC, Wilson R, Wright SC. Properties of inclusive hadron spectra in muon-nucleon scattering at 150 GeV/c. *Phys Rev Letters* 36:1422-1425, 1976.
17. Anderson HL, Bharadwaj VK, Booth NE, Fine RM, Francis WR, Gordon BA, Heisterberg RH, Hicks RG, Kirk TBW, Kirkbride GI, Loomis WA, Matis HS, Mo LW, Myrianthopoulos LC, Pipkin FM, Pordes SH, Quirk TW, Shambroom WD, Skuja A, Verhey LJ, Williams WSC, Wilson R, Wright SC. Measurement of nucleon structure function in muon scattering at 147 GeV/c. *Phys Rev Letters* 37:4-7, 1976.
18. Gragoudas ES, Goitein M, Koehler AM, Verhey LJ, Tepper J, Suit HD, Brockhurst R, Constable IJ. Proton irradiation of small choroidal malignant melanomas. *Am J Ophthalmol.* 83:665-673, 1977.
19. Francis WR, Anderson HL, Bharadwaj VK, Booth NE, Fine RM, Gordon BA, Heisterberg RH, Hicks RG, Kirk TBW, Kirkbride GI, Loomis WA, Matis HS, Mo LW, Myrianthopoulos LC, Pipkin FM, Pordes SH, Quirk TW, Shambroom WD, Skuja A, Verhey LJ, Williams WSC, Wilson R, Wright SC. Diffractive production of mesons by 147-GeV muons. *Phys Rev Letters* 38:633-636, 1977.
20. Anderson HL, Bharadwaj VK, Booth NE, Fine RM, Francis WR, Gordon BA, Heisterberg RH, Hicks RG, Kirk TBW, Kirkbride GI, Loomis WA, Matis HS, Mo LW, Myrianthopoulos LC, Pipkin FM, Pordes SH, Quirk TW, Shambroom WD, Skuja A, Staton MA, Williams WSC, Verhey LJ, Wilson R, Wright SC. Measurement of the proton structure function from muon scattering. *Phys Rev Letters* 38:1450-1454, 1977.
21. Tepper J, Verhey L, Goitein M, Suit HD, Koehler AM. In vivo determinations of RBE in a high energy modulated proton beam using normal tissue reactions and fractionated dose schedules. *Int J Radiat Oncol Biol Phys.* 2:1115-1122, 1977.
22. Suit H, Goitein M, Tepper J, Verhey L, Koehler A, Schneider R, Gragoudas E. Clinical experience and expectation with protons and heavy ions. *Int J Radiat Oncol Biol Phys.* 3:115-125, 1977.
23. Gragoudas E, Goitein M, Koehler A, Wagner M, Verhey L, Tepper J, Suit H, Schneider R, Johnson K. Proton irradiation of choroidal melanomas. *Arch Ophthalmol.* 96:1583-1591, 1978.
24. Gragoudas E, Goitein M, Koehler A, Wagner M, Verhey L, Tepper J, Suit H, Schneider R, Johnson K. Proton irradiation of malignant melanoma of the ciliary body. *Brit J Ophthalmol.* 63:135-139, 1979.
25. Shipley W, Tepper J, Prout G, Verhey L, Mendiondo O, Goitein M, Koehler A, Suit H. Proton radiation as boost therapy for localized prostatic carcinoma. *JAMA* 241:1912-1915, 1979.
26. Verhey L, Koehler A, McDonald J, Goitein M, Ma I-C, Schneider R, Wagner M. The determination of absorbed dose in a proton beam for purposes of charged particle radiation therapy. *Radiat Res.* 79:34-54, 1979.
27. Suit HD, Goitein M, Munzenrider JE, Verhey L, Gragoudas E, Koehler AM, Urano M, Shipley WU, Linggood RM, Friedberg C, Wagner M. Clinical experience with proton beam radiation therapy. *J Canad Assoc Radiol.* 31:35-39, 1980.

Lynn J. Verhey, PhD

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29. Urano M, Goitein M, Verhey L, Mendiondo O, Suit H, Koehler A. Relative Biological effectiveness of a high energy modulated proton beam using a spontaneous murine tumor in vivo. *Int J Radiat Oncol Biol Phys.* 6:1187-1193, 1980.
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32. Verhey LJ, Goitein M, McNulty P, Munzenrider JE, Suit HD. Precise positioning of patients for radiation therapy. *Int J Radiat Oncol Biol Phys.* 8:289-294, 1982.
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39. Urano M, Verhey LJ, Goitein M, Tepper JE, Suit HD, Mendiondo O, Gragoudas ES, Koehler A. Relative biological effectiveness of modulated proton beams in various murine tissues. *Int J Radiat Oncol Biol Phys.* 10:509-514, 1984.
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41. Gragoudas ES, Seddon J, Goitein M, Verhey L, Munzenrider J, Urie M, Suit HD, Blitzer P, Koehler A. Current results of proton beam irradiation of uveal melanomas. *Ophthalmology* 92:284-291, 1985.
42. Austin-Seymour M, Munzenrider JE, Goitein M, Gentry R, Gragoudas E, Koehler AM, McNulty P, Osborne E, Ryugo DK, Seddon J, Urie M, Verhey L, Suit HD. Progress in low LET heavy particle therapy: intracranial and paracranial tumors and uveal melanomas. *Radiat Res.* 104:S219-S226, 1985.

Lynn J. Verhey, PhD

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45. Petti PL, Verhey L, Wilson R. A measurement of w for 150 MeV protons in nitrogen and argon. *Phys. Med. Biol.* 31:1129-1138, 1986.
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Lynn J. Verhey, PhD

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Lynn J. Verhey, PhD

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25. Hwang A, Verhey L, Xia P: Using a Leaf Sequencing Algorithm to Enlarge Treatment Field Length in IMRT presented at the Annual Meeting of the American Association of Physicists in Medicine, Salt Lake City, UT, 2001
26. Poon I, Lee N, Akazawa P, Quivey JM, Verhey L, Xia P: Optimal dose/volume constraints of sensitive structures in inverse planning for nasopharyngeal carcinoma presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, San Francisco, CA, 2001
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28. Pirzkall A, Takahashi M, McKnight TR, Graves EE, Nelson SJ, Verhey LJ, Larson DA, Sneed PK: Metabolic imaging by means of 3D MR-Spectroscopy for low-grade gliomas presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, San Francisco, CA, 2001
29. Xia P, Chuang C, Akazawa P, Phillips TL, Quivey JM, Verhey L, Lee N: Methods of reducing skin toxicity due to extended-field intensity-modulated radiation therapy (EF-IMRT) for the treatment of head and neck cancers presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, San Francisco, CA, 2001
30. Pouliot J, Aubin M, Verhey L, Bani-Hashemi A, Mitschke M, Hernandez P, Hughes J: Low dose megavoltage CT cone beam reconstruction for patient alignment presented at the Annual Meeting of the American Association of Physicists in Medicine, Montreal, Quebec, 2002

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32. Xia P, Yu N, Xing L, Verhey L: Investigation of a variable power objective function for inverse planning optimization in IMRT presented at the Annual Meeting of the American Association of Physicists in Medicine, Montreal, Quebec, 2002
33. Langen K, Pouliot J, Anezinos C, Aubin M, Hsu I, Gottschalk A, Lowther D, Shinohara K, Verhey L, Roach M: Inter-user variability of the BAT ultrasound system presented at the Annual Meeting of the American Association of Physicists in Medicine, Montreal, Quebec, 2002
34. Pirzkall A, Li X, Larson DA, Verhey LJ, Nelson SJ: MR-spectroscopy imaging for resected high-grade gliomas prior to radiation therapy: Tumor extent according to metabolic activity in relation to MRI presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, New Orleans, LA, 2002
35. Xia P, Liu Y, Poon I, Akazawa P, Quivey J, Verhey LJ, Lee N: Development of a standard set of dose constraints to sensitivie structures in treatment of nasopharyngeal cancers using inverse planned IMRT presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, New Orleans, LA, 2002
36. Chuang C, Xia P, Akazawa P, Verhey L, Quivey JM, Lee N: Comparison of three treatment techniques involving IMRT fields for head and neck cancers presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, New Orleans, LA, 2002
37. Langen K, Pouliot J, Anezinos C, Aubin M, Gottschalk AR, Hsu I, Lowther D, Shinohara K, Weinberg V, Verhey LJ, Roach M: Evaluation of the use of the BAT ultrasound system for prostate localization and repositioning: an inter-user study presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, New Orleans, LA, 2002
38. Akazawa C, Akazawa P, Lee N, Quivey J, Verhey L, Xia P: Forward-planned treatment techniques using multisegments for head and neck cancer presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, New Orleans, LA, 2002
39. Pouliot J, Xia P, Aubin M, Verhey L, Langen K, Bani-Hashemi A, Svatos M, Ghelmansarai F, Mitchke M: Dose-guided radiation therapy using low-dose megavoltage cone-beam CT presented at the Annual Meeting of the American Association of Physicists in Medicine, San Diego, CA, 2003
40. Chuang C, Curran B, Verhey L: Clinical implementation and validation of a commercial Monte Carlo dose calculation system presented at the Annual Meeting of the American Association of Physicists in Medicine, San Diego, CA, 2003
41. Lee M, Pirzkall A, Akazawa P, Verhey LJ, Nelson SJ: MR Spectroscopy of radiation effects in healthy brain tissue following radiotherapy presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Salt Lake City, UT, 2003
42. Pouliot J, Xia P, Aubin M, Verhey L, Bani-Hashemi A, Ghelmansarai F, Mitschke M, Svatos M: Low-dose megavoltage cone-beam CT for dose-guided radiation therapy presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Salt Lake City, UT, 2003
43. Lee N, Zhu N, Baker L, Shin EJ, Quivey JM, Phillips TL, Verhey L, Xia P: Intra-fraction patient motion in head/neck cancer patients undergoing intensity-modulated radiation therapy (IMRT) presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Salt Lake City, UT, 2003

Lynn J. Verhey, PhD

44. Park C, Lee N, Kim Y, Quivey JM, Phillips TL, Verhey LJ, Xia P: A method to account for dose fractionation by using a modified equivalent uniform dose algorithm presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Salt Lake City, UT, 2003
45. Aubin M, Roach M, Verhey L, Pouliot J: Clinical acceptance of the flat panel for megavoltage portal imaging at UCSF: Three year experience presented at the Annual Meeting of the American Association of Physicists in Medicine, Pittsburgh, PA, 2004
46. Aubin M, Pouliot J, Milender L, Shinohara, K, Pickett B, Anezinos C, Verhey L, Roach M: Daily prostate targeting with implanted gold markers and an a-Si flat panel EPID at UCSF: A Five year clinical experience presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Atlanta, GA, 2004
47. Lometti M, Thurston D, Aubin M, Verhey L, Lockhart JM, Bland R, Roach M, Pouliot J: Are lateral electronic portal images adequate on-line daily targeting of the prostate? Results of a prospective study presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Atlanta, GA, 2004
48. Chen H, Xia P, Verhey L, Roach III M: Dosimetric consequences to the pelvic lymph nodes due to the daily motion of the prostate presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Atlanta, GA, 2004
49. Xia P, Hsu I-C, Speight J, Ztykovicz A, Gottschalk A, Verhey L: Two isocenter treatment technique for pelvic malignancies with positive pelvic and para-aortic lymph nodes using intensity modulated fields presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Atlanta, GA, 2004
50. Gao M, Perks JR, Kubo HD, Luo C, Skubic SE, Verhey LJ, Smith V, Goetsch SJ, Araki F: The application of newly developed glass rod dosimeter in the quality assurance and dosimetric audit of Gamma Knife presented at the Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Atlanta, GA, 2004

RESEARCH PROGRAM

FIVE SIGNIFICANT RECENT PUBLICATIONS:

1. Xia P, Verhey LJ. MLC leaf sequencing algorithm for intensity modulated beams with multiple static segments. *Medical Physics* 25(8): 1424-1434, 1998

As senior author, I worked closely with Dr. Xia to develop the most efficient general method of leaf segmentation for intensity modulated radiotherapy. This method has been generally accepted by other investigators in the field as the gold standard of leaf segmentation algorithms.

2. Graves EE, Pirzkall A, Nelson SJ, Verhey LJ, Larson DA: Registration of magnetic resonance spectroscopic imaging to computed tomography for radiotherapy treatment planning. *Med. Phys.* 28(12): 2489-2496, 2001

As senior technical author, I developed the data transfer and data verification system for overlaying the Gamma Knife dose distributions from the planning system on the MRSI images as required for accurate correlation of clinical outcome with radiosurgery dose.

3. Xia P, Hwang AB, Verhey LJ: A leaf sequencing algorithm to enlarge treatment field length in IMRT. *Med. Phys.* 29(6): 991-998, 2002

As senior author, I provided the technical guidance to fully understand the problems with the clinical leaf sequencing algorithm and to devise a method to avoid undeliverable sequences through the development of a new computer algorithm.

4. Langen KM, Pouliot J, Anezinos C, Aubin M, Gottschalk AR, Hsu I-C, Lowther D, Liu Y-M, Shinohara K, Verhey LJ, Weinberg V, Roach III M: Evaluation of ultrasound-based prostate localization for image-guided radiotherapy. *Int J Radiat Oncol Biol Phys.* 57(3): 635-644, 2003

As senior technical author, I was heavily involved in the design of the experimental questions and the analysis and interpretation of the data that made this highly controversial and important paper publishable. This study was seminal in showing the superior accuracy of direct radiographic visualization of radiopaque markers in the prostate compared to ultrasound localization.

5. Xia P, Lee N, Liu YM, Poon I, Weinberg V, Shin E, Quivey JM, Verhey LJ: A study of planning dose constraints for treatment of nasopharyngeal carcinoma using a commercial inverse treatment planning system. *Int J Radiat Oncol Biol Phys* 59(3): 886-896, 2004

As senior author, I provided guidance, technical advice and encouragement as well as diplomatic editing that were needed to get this excellent paper published. This paper describes the ultimate method of efficient inverse planning of tumors of the head and neck with intensity modulated radiotherapy (IMRT) and has been responsible for making IMRT of head and neck lesions available to a larger fraction of patients.

CURRENT RESEARCH INTERESTS

1. Precision Radiotherapy.

I am working to improve the applicability, efficiency and safety of intensity modulated x-ray beam treatments (IMRT), planned either with conventional 3DCRT planning programs or inverse treatment planning programs. I have developed collaborations between UCSF and the vendors of these planning programs (NOMOS, Philips) and delivery systems (Siemens) through which we are optimizing the clinical use of IMRT.

Precision treatments require accurate positioning of patient anatomy and accurate localization of the target within the patient on a daily basis. New methods of patient immobilization, position verification and target localization are being developed. The locations of imbedded radiopaque markers are being routinely detected on a daily basis with electronic portal imagers and manually compared with calculated positions from the treatment plan prior to treatment. Work is underway to automate the detection, comparison and required couch motions to allow precise daily positioning of prostate tumors.

The next challenge in positioning is accurate dose delivery to targets that move with respiration. I am establishing a collaboration with a vendor that manufactures implantable radiofrequency transmitters that can be stimulated by external antennas and located by triangulation in real time. I am interested in using this information to move the patient couch or the beam-defining collimator leaves, to keep the target at the treatment isocenter during all phases of the respiratory cycle.

2. Image- and dose-guided radiotherapy

In collaboration with Siemens, we are pursuing the acquisition and manipulation of reconstructed 3D images using a series of images taken rapidly with an electronic portal imager at different gantry angles. These images can be compared with the treatment planning CT on a daily or weekly basis for patient position verification. These 3D images can also be used as a basis for daily analysis of delivered dose. I am working with other faculty and graduate students to develop a method of using this information in an efficient manner to improve the quality of the dose actually delivered to each patient by adjusting treatment plans during a course of treatment if the daily imaging proves that it is necessary.

3. Functional imaging to assist tumor identification.

I am working with other faculty in Radiation Oncology and Radiology to evaluate the use of biological information in the definition of tumor for radiotherapy targeting. Magnetic Resonance Spectroscopy (MRSI) is proving very useful in defining areas of active tumor in prostate and brain. In addition, a state-of-the-art PET-CT scanner is being installed at UCSF in China Basin before the end of 2004. This unit will have the highest spatial resolution currently available for PET information and promises to be extremely helpful in identifying active areas of tumor, particularly for patients with head and neck lesions. I am working to find the best method of transferring and displaying this information for Radiation Oncologists and in evaluating the impact of both PET-CT and MRSI technologies on tumor control.

Exhibit C

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CYTYC SURGICAL PRODUCTS II, INC.

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

11 Xoft Microtube, Inc.,) Case No. CV 05-05312 RMW
12 Plaintiff,)
13 vs.)
14 CYTYC Corporation and Proxima)
Therapeutics, Inc.,)
15 Defendants.)
16 _____)
17 AND RELATED COUNTERCLAIMS)
18 _____)

LLP

1 My name is Lynn J. Verhey. I am a resident of the state of California and am over the age of
 2 18. I am presently employed by the University of California, San Francisco as a Full Professor and
 3 serving as Vice-Chair in the Department of Radiation Oncology. I make the following declaration
 4 based on my personal knowledge, training and experience, and if called upon to testify, I could and
 5 would testify competently to the matters set forth below.

6 **I. INTRODUCTION AND MY EXPERT QUALIFICATIONS**

7 I received my B.A. in Physics from Kalamazoo College, Kalamazoo, Michigan in 1962, and
 8 my M.S. and Ph.D. in Physics in 1964 and 1968, respectively, from the University of Illinois, Urbana,
 9 Illinois. The subject of my research during my education was on the decays of certain charged
 10 particles produced by high energy interactions of protons with Hydrogen and Deuterium.

11 I took a position at UCLA and served as a post-doctoral researcher and Assistant Professor of
 12 Physics from 1968-70, doing experiments at Lawrence Berkeley Laboratory and teaching physics to
 13 undergraduate physics students. I moved to Harvard University in 1970 as an Assistant Professor,
 14 continuing to teach undergraduate physics and perform high energy experiments, this time at Fermi
 15 National Accelerator Laboratory in Illinois. In 1975 I took a position as Hospital Radiation Physicist
 16 at Massachusetts General Hospital (MGH) with a concurrent continuing position as Assistant Professor
 17 at the Harvard Medical School. I then worked with the MGH group to develop and implement proton
 18 radiation therapy as an alternative to x-ray therapy. In 1990, I took the position as Chief of the Physics
 19 Division and Associate Professor in the Department of Radiation Oncology at UCSF. Since that time,
 20 I have continued to serve as Chief of the Physics Division and, in addition, as Vice-Chair of the
 21 Department and as a Full Professor.

22 As part of my responsibilities at UCSF, I have mentored numerous graduate and post-graduate
 23 students, taught an undergraduate class in the Department of Nuclear Engineering at the University of
 24 California, Berkeley (UCB) and graduate classes in the Department of Bioengineering at UCB as well
 25 as at UCSF. I have taught medical physics to medical residents at UCSF as well as to physics
 26 residents. I have performed research on new methods of delivering radiation to cancer patients and
 27 have published over 100 technical papers in this field. I was certified as a therapeutic radiological
 28 physicist by the American Board of Radiology in 1982, appointed a fellow of the American

1 Association of Physicists in Medicine in 2002 and a fellow of the American Society of Therapeutic
 2 Radiology and Oncology in 2006.

3 I am a well-recognized expert in methods of delivering radiation to cancer patients, having
 4 given numerous scientific lectures at scientific meetings, both nationally and internationally. I am
 5 attaching a current copy of my curriculum vitae to this declaration.

6 **II. TOPICS THAT I HAVE BEEN ASKED TO ADDRESS**

7 I have been asked by counsel for Cytac Corporation and Cytac Surgical Products, Inc. to
 8 provide expert testimony relating to United States Patent Nos. 5,913,813 (the "813 patent") and
 9 6,413,204 (the "204 patent"), which are the patents of issue in this lawsuit. The 813 patent describes
 10 and claims an invention in the field of a balloon catheter for treatment of proliferative tissue, while the
 11 204 patent extends this concept to describe and claim as an invention a method for treatment of
 12 proliferative tissue diseases using an interstitial brachytherapy apparatus. These patents describe a
 13 catheter which can be used with an array of radiation-producing materials to irradiate the wall of a
 14 surgical cavity and a defined thickness of tissue beyond that wall, to doses that can both avoid necrosis
 15 of normal tissue and destroy cancer cells that might populate the area. In the case of both the 813 204
 16 patents, I have been asked to provide testimony with respect to the knowledge of people of ordinary
 17 skill in the relevant art and in particular, at the time the described inventions were made, which I
 18 understand to be in the time frame of 1997 to 1999, based on their respective filing dates. I have also
 19 been asked to provide an opinion of how one of ordinary skill in the art would interpret elements of the
 20 claims of the 813 and 204 patents which cover the inventions at issue. I can also provide testimony on
 21 any other background information or technical issue on these patents that the Court may request.

22 **III. INFORMATION CONSIDERED IN FORMING MY OPINIONS**

23 In forming the opinions stated in this declaration, I have reviewed and considered the text of
 24 the 813 patent and the patent history associated with the issuance of the patent as well as the text of the
 25 204 patent and the history associated with its issuance. I have also considered the preliminary claim
 26 construction and identification of extrinsic evidence exchanged by both parties. I have also reviewed
 27 information in "The Physics of Radiation Therapy" (2d edition, 1994) by Faiz Khan, PhD, published
 28 by Williams and Wilkins. I have not reviewed any written or oral opinions from any expert whom

1 Xoft Microtube has retained or may retain in connection with the 813 and 204 patents and I reserve the
 2 right to modify my opinions stated in this declaration after having reviewed any such opinion offered
 3 by any such expert. I also reserve the right to modify my opinions based on any rulings that the Court
 4 might issue in the future relating to these patents.

5 **IV. APPROACH I HAVE USED IN READING THE 813 AND 204 PATENTS AND**
 6 **INTERPRETING THEIR CLAIMS**

7 I understand that the claims of the 813 patent at issue in this lawsuit are claims 1, 2, 3, 4, 8 and
 8 12 found in columns 4, 5 and 6 of the patent. I also understand that the claims of the 204 patent at
 9 issue in this lawsuit are claims 1, 2, 3, 4, 8, 16, 17, 18, 19, 20, 21, 23, 24, 25, 26, 30, 32, 34, 35 and 36
 10 found in columns 8, 9, 10, 11 and 12 of the patent. In the case of patent 813, the claims relate
 11 specifically to subject matter described in columns 1-4, beginning with a summary of the invention and
 12 Figures 1-5, and for patent 204, the claims relate specifically to the discussion in columns 2-8,
 13 beginning with a summary of the invention and Figures 1-7. I understand that a patent claim must be
 14 interpreted in light of the specification of the invention and the illustrative figures which are intended
 15 to describe the invention that is being claimed.

16 I also understand that a claim is to be interpreted from the standpoint of one of ordinary skill in
 17 the art, at the time of the invention, which is approximately when a patent application first describing
 18 the invention was filed. Based on the respective filing dates of the patent applications, I understand the
 19 relevant time frame to be between 1997 and 1999.

20 I understand that patents 813 and 204 can be considered to have a "parent-child" relationship.
 21 Indeed, many of the claims of 204 specifically relate to the same subject matter described in columns
 22 1-4 and figures 1-5 of patent 813. I understand that the proper interpretation of the claims of the 813
 23 and 204 patents also requires analyzing the prosecution history of these two patents, i.e., the public
 24 record of the communications exchanged between the applicants and the United States Patent and
 25 Trademark Office (PTO) leading up the issuance of the 813 and 204 patents, respectively.

26 In understanding and interpreting the claims of the 813 and 204 patents, I have focused on the
 27 specifications and drawing figures in the patents, and the prosecution histories of the 813 and 204
 28 patents. I have read these materials as one of ordinary skill in the art would have read them in the

1 period 1997 to 1999. When appropriate, I have consulted a contemporary reference textbook, which
2 can be helpful in understanding the meaning of a claim term, particularly if the meaning remains
3 unclear after reading the specifications and the prosecution histories.

4 I understand that claim terms are normally used consistently throughout a patent. One has to
5 assign meaning to each and every term in a claim.

6 **V. LEVEL OF SKILL OF ONE OF ORDINARY SKILL IN THE ART**

7 For purposes of interpreting the claims of the 813 and 204 patents, the relevant scientific area is
8 radiation oncology physics, with a focus on brachytherapy. Typically, individuals of ordinary skill in
9 this field would hold a M.S. degree in Physics or Engineering, with 3 or more years of clinical medical
10 physics experience; or a Ph.D. degree in Physics or Medical Physics with 2 or more years of clinical
11 experience.

12 Such a person would have a broad knowledge of the physics of brachytherapy procedures, of
13 the principles of radioactivity and an understanding of the effects of radiation on cells. In addition,
14 such a person would have an understanding of other means of treating cancer cells with radiation such
15 as an external, gantry-mounted linear accelerator. Individuals with such qualifications are considered
16 eligible for certification as a radiation oncology physicist by entities such as the American Board of
17 Radiology and considered capable of working independently in a clinical environment as a medical
18 physicist.

19 **VI. OVERVIEW OF THE INVENTIONS DESCRIBED IN THE 813 AND 204 PATENTS**

20 The claims of the 813 patent relate to the description of an instrument comprising a concentric
21 arrangement of an inner spatial volume and an outer spatial volume defined by an inflatable chamber,
22 disposed near the distal end of a catheter body where one of the volumes can contain a source of
23 radiation, while the other volume would normally contain a radiation absorptive material. In the
24 preferred embodiment, shown in Figure 1 of the patent, the inner volume is an inflatable chamber
25 concentric with the catheter body containing a radioactive source. The outer chamber, concentric with
26 the inner volume, is then inflated with air or other radiation absorbing material, resulting in the wall of
27 the outer chamber being in contact with the outer surface of the surgical cavity at all points. The
28 distance between the radiation source and the wall of the outer chamber can be made constant. This

1 embodiment permits the delivery of radiation to a ring of tissue outside a surgical cavity that is judged
 2 to possibly include cancer cells, and by manipulating the volume and material in the outer chamber, the
 3 ratio of the dose to the surface of the surgical cavity to the dose at the tissue depth where the minimum
 4 dose is prescribed to be received, can be controlled to maximize the effectiveness of the treatment. An
 5 effective treatment could be defined as one that delivers the prescribed dose to the tissue at the depth of
 6 interest, and a dose to tissue between the wall of the surgical cavity and the prescription depth which is
 7 higher, but not likely to necrose healthy tissue.

8 The 813 patent teaches that other embodiments can be used to deliver radiation to proliferative
 9 tissue outside a surgical cavity and these are discussed in 2:64 – 4:20 and supported by figures 3-5.
 10 These other embodiments include the use of a radioactive liquid in an inner inflatable chamber, or a
 11 plurality of radioactive solid particles, a slurry of a fluid containing particles of a radioactive isotope or
 12 a solid radioactive source. In addition, these same radioactive sources can be placed in the space
 13 between the inner inflatable chamber and the outer inflatable chamber. Any of these embodiments
 14 might be used as a means of delivering radiation to a ring of tissue outside the wall of a surgical cavity.

15 The 204 patent, which is a continuation-in-part of the 813 patent, describes an apparatus for
 16 brachytherapy and a method for using it for interstitial delivery of radiation to tissue proximate to the
 17 cavity formed by surgical removal of proliferative tissue. The apparatus includes a catheter body
 18 member having a proximal end and a distal end, an inner spatial volume proximate to the distal end of
 19 the catheter body member, an outer spatial volume defined by an expandable surface element
 20 proximate to the distal end of the body member and surrounding and concentric with the inner spatial
 21 volume. In the usual embodiment of the device, a radiation source is disposed in the inner spatial
 22 volume.

23 The 204 patent describes a number of embodiments that can be used with the device for
 24 delivery of radiation, including radioactive microspheres (Fig. 4), concentric non-spherical chambers
 25 (Fig. 5), a single solid radiation emitting material inside the catheter and an expandable cage defining
 26 the shape of the cavity (Fig. 6), a radioactive fluid filling the outer chamber (Fig. 7a), a radioactive
 27 fluid filling the inner chamber and the outer chamber filled with air or other radiation absorbing
 28 substance (Fig. 7b), and a single solid source in the catheter, surrounded by the outer chamber filled

1 with radiation absorbing substance (Fig. 7c). Figure 7d shows examples of radiation profiles which
 2 might be obtained by the embodiments shown in Fig. 7a – 7c where the depth of interest is shown as 2
 3 cm from the surface of the outer volume. As can be seen, different embodiments can be used to vary
 4 the ratio of the dose at the prescription depth, to the dose at the surface of the cavity.

5 **VII. THE MEANING OF THE DISPUTED CLAIM TERMS IN THE 813 AND 204**
 6 **PATENTS TO ONE OF ORDINARY SKILL IN THE ART**

7 I have reviewed and relied upon the material listed in Section III above. Based upon these
 8 materials, my own knowledge of the technical field to which the patented inventions relate, and my
 9 familiarity with the level of ordinary skill in the art around the time that the 813 and 204 patents were
 10 filed, I have formed opinions as to how one of ordinary skill in the art would have interpreted certain
 11 claim terms at the time of the invention. My opinion of the meaning of each of these disputed terms is
 12 set forth below. I have referenced the materials listed in Section III upon which I have relied for these
 13 opinions. In situations where the disputed claim term is present in both patents 813 and 204, my
 14 interpretation of the term is given only once. The list of disputed claim terms includes those identified
 15 by either party in the case.

16

17 Radionuclide(s) – any radioactive isotope that is unstable and thereby decays into a different
 18 isotope with the emission of radiation (“Physics of Radiation Therapy”, p.12, see 813 2:50 – 2:55 for
 19 examples).

20

21 Means for rendering uniform the radial dose profile – the radial dose profile is defined as the
 22 absorbed dose to tissue as a function of distance from the center of the cavity along a particular
 23 direction of interest. As described in the 813 patent, the points of interest in this profile would be from
 24 the wall of the surgical cavity to a depth somewhat beyond that at which the prescription is defined.
 25 The device provides a means for modifying the ratio of the dose at the depth of interest to the dose at
 26 the surface of the cavity as desired for the particular clinical application, through manipulation of the
 27 quantity and type of substances contained in the spatial volumes as shown in patent 813 Fig. 4 , also
 28 1:59-67.

1
2 Predetermined constant spacing – the spacing between the inner spatial volume and the wall of
3 the outer inflatable chamber can be made constant in all directions if the outer chamber is spherical
4 (Fig. 1 of 813), or constant along a radial direction if non-spherical (see Fig. 3 of 813 and 3:10-13),
5 whenever the outer chamber is inflated.
6

7 Outer closed inflatable chamber – this is a balloon or cage or inflatable chamber of any type
8 that can be made to be in contact with the surface of the surgical cavity when the catheter has been
9 inserted and the chamber is inflated (see 813 2:38-41).
10

11 Inner spatial volume – a region of space which is surrounded by the outer spatial volume
12 defined by a closed inflatable chamber. As shown in Fig. 1 of 813, it can be defined by the wall of an
13 inflatable chamber (see 2:34-36 of 813). As shown in Fig. 5 of 813 and 2:56-67 of patent 813, it can be
14 defined as the region of space containing a radiation source or an array of radiation sources. This is
15 also described in patent 204 2:56-60, 3:58-59, 4:4-7, 4:44-48 and 5:1-6.
16

17 The radioactive material – referred to in claim 8 in 813, this refers to any material containing
18 radionuclides, including microspheres, radioactive fluid or individual solid radioactive particle(s) that
19 can be enclosed in either of the spatial volumes. See patent 813 2:51-67 and 4:46-47.
20

21 Outer spatial volume – a region of space defined by an expandable surface element surrounding
22 an inner spatial volume (see patent 204 2:60-63, 4:4-5 and 8:22-23).
23

24 Brachytherapy – a method of treatment in which radioactive sources are used to deliver
25 radiation at a short distance by interstitial, intracavitary, or surface application (see “The Physics of
26 Radiation Therapy”, p. 418). As used in patent 204, 1:31 – 1:34, it is defined as radiation therapy
27 delivered by a spatially confined radioactive material inserted into the body at or near a tumor or other
28 proliferative tissue disease site

1

2 Intraoperatively – this refers to the fact that the interstitial brachytherapy apparatus is placed
3 into the surgical resection cavity during the operation – i.e., after surgical removal of tumor, but prior
4 to closing the surgical site as indicated in patent 204 7:58 – 7:60.

5

6 Expandable surface element – an expandable or inflatable device such as a balloon or cage that
7 can be expanded or inflated in order to contact the inner surface of the surgical resection cavity (see
8 patent 204 2:61-63).

9

10 Radiation source – any device or material capable of generating radiation, such as radionuclides
11 or a high voltage electronic tube that can produce accelerated electrons which can be used directly to
12 irradiate cells or to produce x-rays through the interaction of these accelerated electrons with a target
13 (see patent 204 1:27-30, 1:47-50, 2:45-46 and 4:10-14).

14

15 Isodose profile – this would usually be a description of the dose received by points in tissue –
16 for example, a plot of dose vs. distance from the center of a source, or plurality of sources. As used in
17 5:12 – 5:41 in patent 204, it refers to 3-dimensional surfaces on which all points receive the same dose.

18

19 Surgical resection – surgical removal of tissue from the body (see patent 204 7:55-58).

20

21 Minimum prescribed dose – the minimum dose needed to destroy existing cancer cells in the
22 opinion of the physician (see line 52 in Fig. 7d of patent 204).

23

24 Configuring the inner and outer spatial volumes to provide minimum prescribed absorbed dose
25 – as defined in claims 1, 19 and 32 of patent 204, where the radioactive material is disposed in the
26 inner spatial volume, the rate at which the dose falls off between the surface of the surgical cavity and
27 the depth at which the minimum dose is to be prescribed, can be controlled by modifying the quantity
28 and type of radiation absorbing material contained within the outer spatial volume. The safe delivery

1 of the minimum prescribed dose at the depth of interest requires that the tissue intervening between the
 2 surface of the cavity and the depth of interest receives a dose which is equal to, or greater than the
 3 prescribed dose but less than that which would necrose (i.e., lethally damage) healthy tissue. See
 4 patent 204 5:22-41 and 6:16 - 7:28.

5

6 Minimum distance outward from the outer spatial volume expandable surface – the target tissue
 7 is defined as that tissue which is between the surface of the inflated outer spatial volume and a
 8 minimum distance outward from that surface, determined by the physician, to include the region in
 9 which tumor cells might reside (see patent 204 6:16-22 and Fig. 7d).

10

11 Providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent
 12 necrosis in healthy tissue – by adjusting the distance between the radiation source and the surface of
 13 the outer spatial volume, or by adjusting the type of radiation absorbing material in the outer spatial
 14 volume, the ratio of the dose at the surface of the outer spatial volume to the dose at the depth of
 15 prescription, can be controlled (see patent 204 6:42 – 7:28 and Figs. 7a – 7d).

16

17 Adapting the expandable surface to contact tissue surrounding the resection cavity to conform
 18 the tissue – the volume of the expandable surface can be adjusted by inflation until the surface of the
 19 expandable volume is in contact with the surface of the resection cavity at all points. In this state, the
 20 shape of the resection cavity conforms to the shape of the expandable surface (see patent 204 5:47-61).

21

22 Desired shape of the expandable surface element – the desired shape of the expandable surface
 23 element is that shape which provides the predetermined constant spacing between the inner spatial
 24 volume and the conformed surface of the resection cavity (see patent 204 5:47-61).

25

26 Delivering a prescribed absorbed dose – once the inflated expandable surface element is in
 27 contact with the surface of the surgical cavity, the dose at the prescription depth can be delivered once
 28 the radiation source is introduced into the catheter (see patent 204 5:66 – 6:28).

1 Inner and outer volumes are configured to provide a minimum prescribed dose - see above.

2
3
4 Controlled dose – refers to controlling the ratio of doses at the depth of prescription to the dose
5 at the surface of the surgical cavity. See patent 204 6:42 – 7:28 and Figs. 7a-7d which show various
6 configurations to deliver minimum prescribed dose with variable doses to the surface of the surgical
7 cavity.

8
9 Reduce or prevent necrosis in healthy tissue proximate to the expandable surface – by
10 controlling the ratio of doses at the depth of prescription to the dose at the surface of the surgical cavity
11 through the use of different amounts and types of radiation absorbers in the inner and outer expandable
12 volumes, necrosis of healthy tissue in the vicinity of the surface of the surgical cavity can be prevented
13 or reduced. See patent 204 6:42 – 7:28 and Figs. 7a-7d which show various configurations to deliver
14 minimum prescribed dose while reducing or preventing necrosis in proximate healthy tissue.

15
16 Predetermined spacing – the spacing between the inner and outer spatial volumes can be set to
17 a predetermined and constant value by modifying the level of inflation or expansion of one or both
18 volumes (see patent 204 5:22-32).

19
20 Interstitial – pertaining to or situated in the interspaces of a tissue. These interspaces are not
21 naturally occurring. See patent 204 1:31-34 and December 20, 2000 amendment at pages 11-15 and
22 “The Physics of Radiation Therapy” at pages 457-458.

23
24 A plurality of radioactive solid particles placed at pre-determined locations within the inner
25 spatial volume to provide a desired composite radiation profile – as shown in Figure 5 of patent 813,
26 and as described in 2:64– 3:9, a plurality of radioactive particles which can be positioned in such a way
27 as to generate a desired dose profile.

1 Interstitial brachytherapy – short distance radiation therapy applied directly into the interspaces
2 of tissue in a cavity that is not naturally occurring (see “Physics of Radiation Therapy” pages 418 and
3 457-458).

4

5 Three-dimensional isodose profile – a three dimensional surface on which the radiation dose is
6 the same at all points (see patent 204 5:16-19).

7

8 Solid radiation source – a radiation source that has a fixed shape and volume and is not
9 deformable (see patent 204 4:44-48 and 4:54-56).

10

11 The prescribed absorbed dose is delivered to the target tissue in substantially three dimensions
12 – as described in claim 18 of patent 204, this refers to the fact that, once the outer chamber is
13 expanded, the tissue surrounding the chamber conforms to the shape of the chamber, thereby assuring
14 that all points in tissue that are a fixed distance from the wall of the surgical cavity will receive the
15 identical dose.

16

17 **Extrinsic Evidence**

18

19 The Physics of Radiation Therapy by Faiz Khan, p. 12 (radioactivity and radionuclides), p. 418
20 (brachytherapy), p. 457-458 (interstitial brachytherapy)

21 **VIII. DEMONSTRATIVES**

22 I understand that I might be requested to provide a tutorial regarding the technology of the 813
23 and 204 patents. I would expect to deliver this information using a combination of Powerpoint slides
24 and photocopied material that I have used previously in the teaching of the Physics of Radiation
25 Oncology to professionals and students.

26 **IX. OTHER CASES IN WHICH I HAVE TESTIFIED DURING THE PAST FOUR YEARS**

27 I have provided testimony as an expert at a deposition in the case of *Maggiani vs. University of*
28 *Southern California* on February 20, 2006.

1 X. COMPENSATION

2 I am being compensated for my work on this matter at a rate of \$500 per hour. My
3 compensation does not depend on the outcome of this case.

4 * * *

5 I declare under penalty of perjury that the foregoing statements are true and correct.

6 Dated: October 12, 2006

San Francisco, California

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8 Lynn J. Verhey, Ph.D.
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EXHIBIT I

#7/A



PATENT APPLICATION

OUR FILE NO. 970344.0RI

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re App : Jeffery A. Williams, et al.
S.N. : 08/900,021 : September 1, 1998
Filed : July 24, 1997 : Art Unit 3736
For : DOUBLE WALL BALLOON CATHETER
FOR TREATMENT OF
PROLIFERATIVE TISSUE : Examiner J. Lacyk

ASSISTANT COMMISSIONER FOR PATENTS

WASHINGTON, D.C. 20231

Dear Sir:

Responsive to the first Official Action of May 12, 1998,
please amend the above-captioned application as follows:

IN THE CLAIMS:

Please cancel Claim 12.

Please amend the following claims:

1 (Amended). Apparatus for delivering radioactive emissions to a body location with a [controlled] uniform radiation profile, comprising:

(a) a catheter body member having a proximal end and distal end;

(b) an inner spatial volume disposed [at] proximate the distal end of the catheter body member;

(c) an outer, closed, [distensible] inflatable, chamber defined by a radiation transparent wall [disposed at]

affixed to the body member proximate the distal end [of the body member] thereof in surrounding relation to the inner spatial volume with a predetermined constant spacing between said inner spatial volume and the radiation transparent wall;

A1 (d) a material containing a radionuclide(s) disposed in one of the inner spatial volume and outer chamber; and

(e) means disposed in the other of the inner spatial volume and outer chamber for [controlling] rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber containing the radionuclides.

2 (Amended). The apparatus as in Claim 1 wherein said inner spatial volume is an inner closed, [distensible] chamber defined by a further radiation transparent wall.

3 (Amended). The apparatus of Claim 1 wherein the means for [controlling] rendering uniform the absorbed dose profile is a radiation attenuating material.

4 (Amended). The apparatus of Claim [2] 3 wherein the radiation [absorbing fluid] attenuating material is selected from a group consisting of barium sulphate, water, and X-ray contrast media.

8 (Amended). The apparatus as in Claim [1] 2 wherein the A2 inner chamber contains the radioactive material.

10 (Amended). The apparatus as in [any one of Claims 7 or] A3 Claim 8 wherein the radioactive material is a fluid.

11 (Amended). The apparatus as in [any one of Claims 7 or]
A4 Claim 8 wherein the radioactive material is a solid.

12 13 (Amended). The apparatus as in Claim 1 wherein the
material containing a radionuclide comprises a plurality of
radioactive solid particles [are] placed at predetermined
locations within the inner spatial volume to provide a desired
composite radiation profile.

Please add the following claim:

13 14. The apparatus as in Claim 2 wherein the inner and outer
chambers are spherical in shape and are concentric.

R E M A R K S

This Amendment is submitted in response to the first
Official Action of May 12, 1998.. Reconsideration and allowance
of Claims 1-11 and 13, as presently amended, are respectfully
requested.

The present invention is directed to an apparatus for
treating proliferative tissue disorders by delivering radioactive
emissions to target tissue within the body with a uniform radial
absorbed dose profile whereby diseased tissue may be irradiated
with sufficient intensity to kill disease cells, but without
producing necrosis of neighboring healthy tissue. With the
apparatus of the present invention, it is possible to deliver a
desired radiation dose at a predetermined radial distance from a
source of radioactivity by providing a catheter body member
having an inner spatial volume disposed proximate the distal end
of the catheter body and with an outer, closed, inflatable,

chamber defined by a radiation transparent wall affixed to the body member proximate the distal end thereof in a surrounding relation to the inner spatial volume with a predetermined constant spacing between the inner spatial volume and the radiation transparent wall. A material containing a radionuclide is introduced through the catheter body in either the inner spatial volume or the outer chamber and the other of the inner spatial volume or outer chamber not containing the radionuclide is made to contain a radiation attenuating material for rendering uniform the radial absorbed dose profile of the emissions from the one of the inner spatial volume and outer chamber that contains the radionuclide.

In the Official Action, objection was raised to Claims 4 and 13 under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 13 has been amended to clarify that the material containing a radionuclide as recited in claim 1 comprises "a plurality of radioactive solid particles". Claim 4 has been amended by changing "radiation absorbing fluid" to -- radiation attenuating material --, the latter phrase finding an antecedent in Claim 3 from which it now depends.

Concerning the rejection on the merits, Claims 1-5, 8 and 10 were rejected under 35 U.S.C. §102(b) as being anticipated by Ishiwara et al. This rejection is respectfully traverse. Before it is appropriate to find a claim anticipated under 35 U.S.C. §102(b), it is necessary to find within the four corners of the prior art reference relied upon a full teaching of each and every

element of the claims sought to be anticipated. As Claim 1 has now been amended, it calls for an outer, closed, inflatable chamber located proximate the distal end of a catheter body member in surrounding relation to an inner spatial volume such that there is a predetermined constant spacing between the inner spatial volume and the radiation transparent wall. There is then provided a means disposed in the chamber, not having the radiation source, a substance for rendering uniform the radial absorbed dose profile of the emissions from the chamber that contains the radiation source. In the Ishiwara et al. '360 patent relied upon for anticipation, the outer chamber defined by the radiation transparent wall 12 cannot provide a uniform radiation profile. The outer balloon 12 in the Ishiwara et al. patent functions only to stabilize the device within and hold a thermal mass (liquid) against surrounding tissue so that it can be warmed or cooled by thermal conduction. There is no teaching or suggestion in the patent of how to provide a uniform radial absorbed dose profile of emissions emanating from the liquid radiation source 38. Moreover, given the banana shape of the Ishiwara device, the profile will be much different proximate the distal and proximal ends of the balloon 12 than in its central tissue contacting region. Thus, it cannot be said that applicants' invention, as claimed, is taught by or inherent in the Ishiwara '360 device.

Given the above mentioned differences, neither Claim 1 nor any of the remaining dependent claims is anticipated by the

Ishiwara et al. teachings. It is further submitted that the invention of Claim 1 is not rendered obvious from the teachings of the Ishiwara et al. patent.

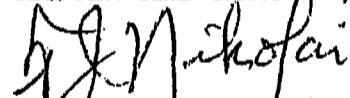
While admittedly the present invention and the device described in the Ishiwara et al. patent have some points of similarity, i.e., both are catheters having an outer closed inflatable chamber and an inner spatial volume surrounded by the outer chamber and both are designed to provide radiation therapy to a tumor site, that is where the similarity ends. Applicants' invention is specifically designed to provide a uniform radial absorbed dose profile of the emissions from the particular chamber containing the radionuclide material so that occurrences of "hot spots" and/or "cold spots" are substantially eliminated. Hot spots can result in necrosis of healthy tissue, a condition to be avoided, while cold spots may mean that cancerous cells are not irradiated and killed. In one embodiment, uniformity of the radial absorbed profile is achieved by providing a spherical outer chamber which when inflated to contact the margins resulting following surgical removal of the tumor, a desired constant spacing will be maintained between the radiation source and the adjacent tissue structures. In a second embodiment, attention is paid to the spacing between the inner and outer radiation transparent walls so that it is constant over the entire surfaces of the two chambers. Given these important distinctions which are neither taught nor suggested by the Ishiwara reference, applicants' independent Claim 1, as amended,

is not made obvious from the prior art. In fact, it is proper to say that the Ishiwara et al. reference teaches away from applicants' invention given the elongate, cylindrical shape of the radiation source employed and the oblong-shaped outer balloon surrounding it.

In that Claim 1, as amended, has been shown to be patentable over the prior art, and because Claims 2-11 and 13 depend directly or indirectly from Claim 1, all of the claims remaining in the application are believed to be in condition for allowance and a Notice to that effect is respectfully solicited.

Respectfully submitted,

HAUGEN AND NIKOLAI, P.A.


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Phone: 612-339-7461

CERTIFICATE OF MAILING

I hereby certify that the foregoing Amendment in response to the Official Action of May 12, 1998 in application Serial No. 08/900,021 of inventors, Jeffery A. Williams et al., filed July 24, 1997, for "DOUBLE WALL BALLOON CATHETER FOR TREATMENT OF PROLIFERATIVE TISSUE" is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on September 1, 1998.

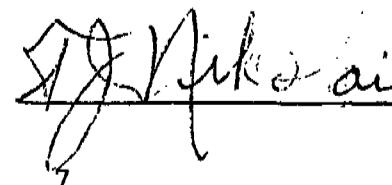


EXHIBIT J

OPIE SCHOO
PATENT OFFICE
MAR 11 2002

COPY OF PAPERS
ORIGINALLY FILED

Docket No.: 101360-16
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Rance A. Winkler, et al.

Application No.: 09/464,727-7988

Group Art Unit: 3736

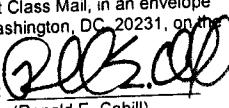
Filed: December 16, 1999

Examiner: J. Lacyk

For: ASYMMETRIC RADIATION DOSING
APPARATUS AND METHOD

I hereby certify that this correspondence is being deposited with the U.S.
Postal Service with sufficient postage as First Class Mail, in an envelope
addressed to: Commissioner for Patents, Washington, DC 20231, on the
date shown below.

Dated: 2/27/02

Signature: 
(Ronald E. Cahill)

AMENDMENT

Commissioner for Patents
Washington, DC 20231

Dear Sir:

In response to the Office Action dated October 31, 2001 (Paper No. 5), please amend the above-identified U.S. patent application by replacing all of the claims with the Clean Copy of All Pending Claims below. A Complete Set of Pending Claims With Markings to Show Amendments Made is attached to this Amendment following the signature page.

03/14/2002 0817H181 00000019 09464727

01 FC:210

11.00 0P

03/14/2002 0817H181 00000019 09464727
02 FC:202
84.00 0P

Application No.: 09/464,727-7988

Docket No.: 101360-16

Clean Copy of All Pending Claims

1. (Amended) An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:
 - an expandable outer surface defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;
 - a radiation source disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume, the radiation source further being asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves with respect to the apparatus volume.
2. (Amended) A surgical apparatus for providing radiation treatment to target tissue comprising:
 - an expandable outer surface defining an apparatus volume;
 - a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of solid radiation sources being provided in a spaced apart relationship on a single elongate member, the single elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources with respect to a longitudinal axis through the apparatus volume.
3. The apparatus of claim 2, further comprising a catheter in communication with the apparatus volume, the elongate member extending through the catheter into the apparatus volume.
4. The apparatus of claim 3, wherein the elongate member is formed of a shape memory alloy, the elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources, taking on a substantially straight shape while being inserted through the catheter to the apparatus volume, and resuming an asymmetric shape when extended into the apparatus volume.

Application No.: 09/464,727-7988

Docket No.: 101360-16

5. (Amended) A surgical apparatus for providing radiation treatment to target tissue comprising:
an expandable outer surface defining an apparatus volume;
a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, wherein at least one of the plurality of solid radiation sources has a different specific activity from at least one other solid radiation source.

6. (Amended) A surgical apparatus for providing radiation treatment to target tissue comprising:
an expandable outer surface defining an apparatus volume;
a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of radiation sources being provided on at least two elongate members extending into the apparatus volume, at least one of the elongate members being shaped to provide asymmetric placement of a radiation source with respect to a longitudinal axis through the apparatus volume.

7. The apparatus of claim 6, wherein each of the at least two elongate members includes a plurality of solid radiation sources provided in a spaced apart relationship.

8. The apparatus of claim 1, wherein the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth.

9. (Amended) An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:
an expandable outer surface having a base and defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

Application No.: 09/464,727-7988

Docket No.: 101360-16

a radiation source disposed completely within and spaced apart from the expandable outer surface; and

an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with respect to the apparatus volume.

10. (Amended) The apparatus of claim 9, wherein the asymmetric radiation shield comprises a radio-opaque material disposed on only a portion of the expandable outer surface.

11. The apparatus of claim 10, wherein the expandable outer surface comprises an inflatable balloon.

12. The apparatus of claim 11, wherein the radiation shield comprises a barium material disposed a portion of the inflatable balloon.

13. The apparatus of claim 9, further comprising at least one radiation shield extending from the base of the expandable outer surface toward an opposite end of the expandable surface, the shield being in between and spaced apart from the radiation source and the expandable outer surface, the shield forming a radio-opaque barrier between a portion of the radiation source and the target tissue.

14. The apparatus of claim 13, wherein the radiation shield comprises two shields provided on opposite sides of the radiation source.

15. Canceled.

16. Canceled.

17. Canceled.

18. Canceled.

Application No.: 09/464,727-7988

Docket No.: 101360-16

19. Canceled.

Application No.: 09/464,727-7988

Docket No.: 101360-16

REMARKS/ARGUMENTS

Applicants appreciate the Examiner's indication that claims 2 through 7 define allowable subject matter. Applicants have amended claims 2, 5 and 6 to be independent claims including the recitations of the base claim and any intervening claims and to correct any rejections under 35 U.S.C. § 112, second paragraph. Applicants have also amended the preamble to read that the recited apparatus is a surgical apparatus for providing radiation treatment to target tissue. This amendment is supported in the opening paragraph of the Detailed Description of the Invention.

Applicants have amended independent claim 1 (from which claim 8 depends) and independent claim 9 (from which claims 10 to 14 depend, directly or ultimately) to better define the invention. Applicants have also amended claim 10 to recite that radio-opaque material is disposed **only** on a portion of the expandable surface. Applicants cancel claims 15 to 19 herein. Accordingly, claims 1 to 14 are now pending.

Claim Rejections Over McGrath

Claims 1 and 9 stand rejected as anticipated by McGrath (US 6,036,631) under 35 U.S.C. § 102(e). In particular, the Examiner states that "McGrath et al discloses a device for treating tissue having an expandable outer surface and a radiation source disposed within the expandable surface having a plurality of solid radiation sources (Fig. 2B). McGrath et al also teaches the use of shielding to absorb some of the radiation."

McGrath is directed to a device and method for treatment of cancerous tissue from a body conduit, i.e., interluminal treatment. By contrast, Applicants' apparatus is an interstitial brachytherapy apparatus, used to treat remaining proliferative tissue surrounding a surgical extraction site such as might be found in the treatment of brain or breast cancers. As a result of this difference in purpose, there are a number of key differences in structure between McGrath and claims 1 and 9.

For example, the expandable outer surface of claims 1 and 9 defines a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated. (See Page 7, lines 8 to 15.) Further, the radiation source is disposed completely within the expandable surface and is spaced apart from the apparatus volume. (See Page 8, line 23 to page 9 line 13, noting the

Application No.: 09/464,727-7988

Docket No.: 101360-16

advantages of providing the radiation source within the interstitial volume and spaced apart from the target tissue; See also each of FIGS. 1 and 3 through 9, showing the radiation sources disposed entirely within the expandable surface). Further with respect to claim 1, the radiation source is located and arranged within the expandable outer surface so as to create asymmetric radiation isodose curves with respect to the apparatus volume. (See Page 9, line 23 to page 10, line 7.) That is, the radiation source is arranged within the device so that asymmetric dosing appears at the apparatus volume, which is configured to correspond to the interstitial void created by surgical extraction of diseased tissue.

The device of McGrath is not configured for use interstitially, it is configured for use interluminally, with balloons provided only to hold its catheter within a lumen, or to dilate the lumen. Accordingly, the radiation source in McGrath is not located completely within any of the disclosed balloons, nor is it located and arranged to provide an asymmetric dose at an apparatus volume that conforms to an interstitial void. Rather, McGrath provides an x-ray tube 48 that slides within a catheter, or a plurality of radiation-emitting seeds 52 "essentially forming a linear source." (Column 5, lines 34 to 37.) Accordingly, McGrath lacks several of the features recited in claim 1.

McGrath also lacks the features recited in claim 8 which depends from claim 1. Claim 8 recites that the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth. That is, the expandable outer surface actually causes the interstitial void to take on the same shape as the apparatus volume so that, even for oddly shaped voids in soft tissue, the shape of the target tissue that is to receive the asymmetric radiation dose will be the same as for the apparatus volume, enabling precise delivery of prescription doses of radiation asymmetrically from Applicants' claimed configuration.

As described above, McGrath does not disclose, teach or suggest the configuration that is recited in claim 9 that is also recited in claim 1. In addition to the structure it recites in common with claim 1, claim 9 recites an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with

Application No.: 09/464,727-7988

Docket No.: 101360-16

respect to the apparatus volume. No portion of McGrath provides an outer expandable surface defining such an apparatus volume, and, while other configurations are referred to generically, the shielding that is provided by McGrath is simply a tubular shield that protects the bladder neck and sphincter. (See, Column 10, lines 7 to 39.) Nowhere does McGrath disclose, teach or suggest providing asymmetric shielding spaced apart from a radiation source so as to create predetermined asymmetric isodose curves with respect to an apparatus volume defined by the outer expandable surface.

Claim Rejections Over Ciezki in view of Apple

Claims 1 and 8 to 14 stand rejected as unpatentable over Ciezki (EP 0 867 200) in view of Apple (WO 99/33515) under 35 U.S.C. § 103. In particular, the Examiner states that:

Ciezki et al teaches a treatment device having a plurality of radiation sources disposed in a catheter. Ciezki et al also teaches the use of shielding or an attenuator made from a radio-opaque material i.e. tantalum. Ciezki et al teaches the claimed device except for the use of an inflatable balloon catheter or the specific use of barium as the shielding material. Apple et al teaches a radioactive treatment device that uses an inflatable balloon to place the catheter at the treatment site. . . . Therefore a modification of Ciezki et al such that the catheter includes an inflatable balloon would have been obvious to help in the placement and retention of the catheter at the treatment site;

The combination of Ciezki and Apple suffers from all of the same problems as McGrath does. Regarding claim 1, the Examiner recognizes that Ciezki does not provide an expandable outer surface defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated; and a radiation source disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume. Apple does not fill in this missing teaching. Apple is directed to a catheter apparatus that is filled with a radioactive gas. The catheter can be used to treat restenosis after angioplasty, or it can treat malignancies. The “restenosis” configuration includes a number of balloons of the type generally used to hold a catheter in an artery; that is, interlumenally. None of these balloons define an apparatus volume within an interstitial void within which the radioactive source is completely placed. Even where Apple discloses a device for interstitial use (See, e.g., FIGS. 17 to 19), the radiation source completely fills the balloon and is not in a spaced apart relationship from the balloon as is recited in claim 1. Thus, even if a balloon from Apple were added to Ciezki, the configuration of claim

Application No.: 09/464,727-7988

Docket No.: 101360-16

1 would not result.

More significantly, neither Apple nor Ciezki nor their combination teaches asymmetric placement of a radiation source that is completely within an expandable surface defining an apparatus volume so as to result in asymmetric radiation isodose curves with respect to the apparatus volume. As described above and in the portions of the application cited above, Applicants' configuration provides significant advantages in the treatment of marginal proliferative tissue surrounding an interstitial void left by a surgical tumor resection. Accordingly, neither Ciezki nor Apple nor their combination renders the subject matter of claim 1 unpatentable to Applicants. Claim 8, which depends from claim 1, is further patentable over Ciezki and Apple because neither teaches or suggests the recitations of claim 8 for the same reasons as described above with respect to McGrath.

As described above, neither Ciezki nor Apple nor their combination discloses, teaches or suggests the configuration that is recited in claim 9 that is also recited in claim 1 – that is, an expandable outer surface having a base and defining a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated; and a radiation source disposed completely within and spaced apart from the expandable outer surface.

In addition to the structure it recites in common with claim 1, claim 9 recites an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves with respect to the apparatus volume. No portion of Ciezki defines such an apparatus volume and the only embodiment of Apple that provides an apparatus volume (FIGS 17 to 19) does not include any shielding. Where Ciezki and Apple do provide shielding, it is to protect blood flowing through the apparatus as it irradiates an aterial wall. The disclosed shielding does not provide asymmetric radiation dosing with respect to an expandable outer surface defining an apparatus volume, because there is no such volume in these references. As described above and in the portions of the application cited above, Applicants' configuration with asymmetric shielding provides significant advantages in that it provides precise delivery of prescription doses of radiation asymmetrically about an interstitial void created by surgical resection of diseased tissue. Neither of these references, alone or

Application No.: 09/464,727-7988

Docket No.: 101360-16

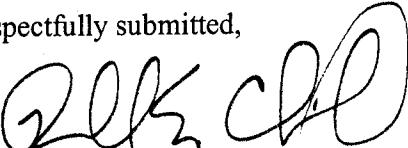
combined, teach or suggest a device that achieves this result.

Conclusion

For all of the foregoing reasons, Applicants request that the Examiner reconsider the application and allow each of claims 1 to 14 to issue. If the Examiner believes that an interview would facilitate the resolution of any outstanding issues, the Examiner is kindly requested to contact the undersigned.

Dated: 2/27/02

Respectfully submitted,

By 

Ronald E. Cahill

Registration No.: 38,403

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Application No.: 09/464,727-7988

Docket No.: 101360-16

Complete Set of Pending Claims With Markings to Show Amendments Made

1. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

an expandable outer surface defining [an] a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

a radiation source [replaceably disposable] disposed completely within the expandable outer surface and located so as to be spaced apart from the apparatus volume, the radiation source [comprising a plurality of solid radiation sources arranged] further being asymmetrically located and arranged within the expandable surface to provide predetermined asymmetric isodose curves [within the target tissue] with respect to the apparatus volume.

2. [The apparatus of claim 1, wherein a] A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of solid radiation sources [are] being provided in a spaced apart relationship on a single elongate member, the single elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources with respect to a longitudinal axis through the apparatus volume.

3. The apparatus of claim 2, further comprising a catheter in communication with the apparatus volume, the elongate member extending through the catheter into the apparatus volume.

4. The apparatus of claim 3, wherein the elongate member is formed of a shape memory alloy, the elongate member being shaped to provide asymmetric placement of the spaced apart solid radiation sources, taking on a substantially straight shape while being inserted through the

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Application No.: 09/464,727-7988

Docket No.: 101360-16

catheter to the apparatus volume, and resuming an asymmetric shape when extended into the apparatus volume.

5. [The apparatus of claim 1,] A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, wherein at least one of the plurality of solid radiation sources has a different specific activity from at least one other solid radiation source.

6. [The apparatus of claim 1, wherein] A surgical apparatus for providing radiation treatment to target tissue comprising:

an expandable outer surface defining an apparatus volume;

a radiation source replaceably disposable within the expandable outer surface, the radiation source comprising a plurality of solid radiation sources arranged to provide predetermined asymmetric isodose curves within the target tissue, the plurality of radiation sources [are] being provided on at least two elongate members extending into the apparatus volume, at least one of the elongate members being shaped to provide asymmetric placement of a radiation source with respect to a longitudinal axis through the apparatus volume.

7. The apparatus of claim 6, wherein each of the at least two elongate members includes a plurality of solid radiation sources provided in a spaced apart relationship.

8. The apparatus of claim 1, wherein the expandable outer surface is sufficiently rigid to deform the target tissue into the shape of the expandable outer surface, causing the predetermined asymmetric isodose curves to penetrate into the target tissue to a prescribed depth.

9. An interstitial brachytherapy apparatus for treating target tissue surrounding a surgical extraction comprising:

Application No.: 09/464,727-7988

Docket No.: 101360-16

an expandable outer surface having a base and defining [an] a three-dimensional apparatus volume configured to fill an interstitial void created by the surgical extraction of diseased tissue and define an inner boundary of the target tissue being treated;

a radiation source [replaceably disposable] disposed completely within and spaced apart from the expandable outer surface; and

an asymmetric radiation shield spaced apart from the radiation source, the asymmetric radiation shield providing predetermined asymmetric isodose curves [within the target tissue] with respect to the apparatus volume.

10. The apparatus of claim 9, wherein the asymmetric radiation shield comprises a radio-opaque material disposed on only a portion of the expandable outer surface.

11. The apparatus of claim 10, wherein the expandable outer surface comprises an inflatable balloon.

12. The apparatus of claim 11, wherein the radiation shield comprises a barium material disposed a portion of the inflatable balloon.

13. The apparatus of claim 9, further comprising at least one radiation shield extending from the base of the expandable outer surface toward an opposite end of the expandable surface, the shield being in between and spaced apart from the radiation source and the expandable outer surface, the shield forming a radio-opaque barrier between a portion of the radiation source and the target tissue.

14. The apparatus of claim 13, wherein the radiation shield comprises two shields provided on opposite sides of the radiation source.

15. Canceled.

16. Canceled.

17. Canceled.

18. Canceled.

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Application No.: 09/464,727-7988

Docket No.: 101360-16

19. Canceled.

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12 NORTHERN DISTRICT OF CALIFORNIA
13 SAN JOSE DIVISION

14 HOLOGIC, INC., CYTYC CORPORATION,
and HOLOGIC L.P.,

Case No. C08 00133 RMW (RS)

15 Plaintiffs,

MANUAL FILING NOTICE

16 vs.

Date: June 25, 2008

17 SENORX, INC.,

Time: To Be Set

18 Defendant.

Room: Courtroom 6, 4th Floor

Judge: Hon Ronald M. Whyte

20 AND RELATED COUNTERCLAIMS.

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Regarding: Exhibits E and G to the Declaration of Katharine L. Altemus in Support of Plaintiffs' Opening Claim Construction Brief

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[X] Item Under Seal

Dated: May 21, 2008

HOWREY LLP

By: /s/
Katharine L. Altemus

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